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THE NUMBER OF ISOTOPES AS A FUNCTION OF THE ATOMIC WEIGHTS OF THE ELEMENTS

E. P. Ozhigov

D.I. Mendeleev attached great importance to the ratios between the atomic weights of neighboring elements and element-analogs: in some regularities found by earlier and contemporary workers he saw the "seeds" of the periodic law [1].

Investigations aiming at an explanation of the ratios between atomic weights of neighboring elements were undertaken by several workers [2,3,4] and some of these studies [3,4] make a definite contribution to certain aspects of nuclear periodicity.

In the present paper an attempt is made to establish a functional dependence between the number of isotopes in the periods and the mean values of the differences of the atomic weights of the elements.

If such a dependence could be established, it would permit the prediction of the number of isotopes in a given part of the periodic system.

In view of the fact that a close genetic bond exists between neighboring and closely located elements of the periodic system, as evidenced by the isotopic composition of these elements [5], we have utilized in our calculations not the difference between neighboring elements but the averaged difference within the Mendeleev periods. The presence of nuclear periodicity of the Mendeleev type [2] is adequate theoretical justification for such a procedure.

In our calculations the limits of the periods were defined as the magnitudes obtained as the arithmetic mean between the atomic weights of the inert gases and the alkali metals. An exception is made for the end of the sixth and the start of the seventh periods where, due to the absence of element 87 in nature, the dividing boundary was assumed to be the atomic weight of radon.

The mean difference per element was obtained by dividing the length of the period in units of atomic weight by the number of elements. The neutron was assumed to be an element and was taken into account in calculating the mean atomic difference of the first period.

Analysis of the data brought to light an interesting dependence, involving the close similarity between the values of $\underline{R}^r$ and the mean number of isotopes of the individual elements.

The calculations and literature data are presented in Table 1 from which we see that the number of isotopes in the periods known at the present time approximates the number found by the formula $\underline{N} \cdot \underline{R}^r$ (where $\underline{N}$ is the number of elements in a period, $\underline{R}$ is the mean difference per element, and $\underline{r}$ is the exponent equal to $\underline{R}$.

The poorest agreement in the number of isotopes occurs in the sixth period. This might be due to the isotopic composition of all the elements of this period having still been studied inadequately. We may expect, in fact, the discovery of a considerable number of new isotopes in this part of the periodic system.

The physical significance of the expression $\underline{R}^r$ may be revealed by analysis of the series of isotopes of individual periods. By an empirical method the author derived a rule which states that the number of isotopes in a period may be calculated from the formula $\underline{N} \cdot \underline{L}^2$, where $\underline{N}$ is the number of elements and $\underline{L}$ is the mean tabular difference per element:

$$L = \frac{\text{series of isotopes of the period in mass numbers}}{\text{number of elements in the period}}$$

TABLE 1

Periods	Series of elements	Limits of periods (ends)	Length of period (in units of atomic wt.)	R	Numerical value of R^r	No. of isotopes in periods: Calcd. from formula $N \cdot R^r$	No. of isotopes in periods: found (Shpolsky [6])
1	H—He	5.47	5.47	1.82	2.97	6* + n = 7	6 + n = 7
2	Li—Ne	21.59	17.12	2.14	5.10	41	36
3	Na—Ar	39.60	19	2.37	7.73	62	45
4	K—Kr	84.59	46	2.55	10.88	196	173
5	Rb—Xe	132.10	48.51	2.69	14.32	256	217
6	Cs—Rn	222	90.90	2.84	19.38	620	296
7	Fr—U	238.53	17.53	2.50**	9.95	119**	80***
				Total		1301	854

* Calculation performed for two elements, since the neutron does not form isotopes.

** Since the isotopic composition of the elements of the end of the periodic system has not been completely established, the value of R is calculated from the first seven elements (including Np) and is extended over the whole 12 (including 97 and 98).

*** Isotopes of elements 97 and 98 are taken into account [7].

TABLE 2

Magnitudes compared	Periods: 1	2	3	4	5	6	7
Atomic difference per element	2.00	2.25	2.55	3,30	3.50	2.90	2.2
"Isobaric number" per element	1.50	2.13	2.58	3.24	4.18	2.90	1.9

For example, the series of isotopes of the second period Li^6—Ne^{23} has a period length of 18. The mean difference per element in units of atomic weight is 2.25. The number of isotopes according to the formula $\underline{N} \cdot \underline{L}^2$ is 41, which is close to the number of isotopes found for this period (36). An explanation was later given of this empirical formula by comparing the magnitude of the mean tabular difference per element with our "isobaric number", which can be carried out fairly simply. For example, lithium has two stable isotopes, Li^6 and Li^7, the isotopes He^6 and Be^7 of shorter life periods will be related to the isotopes of lithium by the isobars:

$$\text{"Isobaric number" of lithium} = \frac{2+2}{2} = 2.$$

TABLE 3

Periods	Series of isotopes of the elements of a period	Number of isotopes: Predicted from formula $N \cdot L^2$ in 1946 [8]	Found in 1948 [9]	Calc'd from Petrovich's tables in 1948 [9]	Found in 1950 [6]
1	n(H)—He	8	6 + n	8	6 + n
2	Li—Ne	45	33	36	36
3	Na—Ar	50	44	54	45
4	K—Kr	140	157	200	173
5	Rb—Xe	167	206	227	217
6	Cs—Rn	276	246	270	296
7	Fr—U	44	40	84*	80
	Total	720	733	879	854

On summing the "isobaric numbers" of the stable isotopes of the elements of the second period and dividing the result by the number of these isotopes, we obtain a value of 2.125 for the "isobaric number" of the elements of the second period, which is close to the mean atomic difference per element for this period. "Isobaric numbers" for all the periods, taken from Petrovich's tables [9], are set out in Table 2.

* Calculated for the series Fr—U and extended over the 12 elements.

This table directly reflects the proportional dependence of the isobaric numbers on the number of isotopes entering into a series.

Hence we may assume that the magnitude $\underline{L}^2$ or $\underline{L}_1 \cdot \underline{L}_2$ consists of the atomic difference per element and the "isobaric number" of both magnitudes calculated for the period.

By utilizing the formula $\underline{N} \cdot \underline{L}^2$ we succeeded in showing the trend and number of isotopes discovered in recent years.

Table 3 illustrates the good agreement of the number of calculated isotopes with the number subsequently found by experiment.

A defect of the formula $\underline{N} \cdot \underline{L}^2$ is that the number of isotopes calculated with its help is dependent on variables—the discovered isotopes of the alkali metals and of the inert gases.

Comparison of the number of isotopes found by the formulas $\underline{N} \cdot \underline{L}^2$ and $\underline{N} \cdot \underline{R}^r$ leads to the assumption that the expression $\underline{N} \cdot \underline{R}^r$ to a certain approximation expresses the limiting number of isotopes in the periods (without nuclear isomers).

This observation is also grounded in the fact that in the upper part of the periodic system the isotopic composition of many elements has remained nearly constant over a period of years; in the region of the pleiads, in fact, a regular transition is observed from the poorly stable β^+ active isotopes to the stable ones and then to the poorly stable β^- active isotopes.

Consequently, it appeared possible to derive a general formula for calculation of the number of possible isotopes in a given part of the periodic system.

This formula will have the following form:

$$S = 2R_1^{r_1} + 8(R_2^{r_2} + R_3^{r_3}) + 18(R_4^{r_4} + R_5^{r_5}) + 32R_6^{r_6} + N_7 \cdot R_7^{r_7},$$

where $\underline{R}$ is the mean atomic difference per element for the periods designated by exponents, $\underline{r}$ is the exponent equal to $\underline{R}$, $\underline{N}$ is the number of elements in the seventh period, equal to 12 at the present time.

The physical significance of the expression $\underline{R}^r$ is the product of $\underline{R}$ and the possible "isobaric number" which approximates to $\underline{R}$ (Table 4)

TABLE 4

Periods	Mean no. of isotopes in the pleiad of the element	Isobaric No.	Calc'd no. of isotopes per element	
			Isobaric number · R	$\underline{R}^r$
1	3	1.5	2.73	2.93
2	4.5	2.13	4.45	5.10
3	5.63	2.26	6.27	7.73
4	9.25	3.55	8.97	10.88
5	12.05	4.59	12.34	14.32
6	9.25	3.54	10.05	19.34
7	7.5	3.30	8.25	9.95

SUMMARY

1. It is established that the possible number of isotopes in the periods is a function of the magnitude of the mean atomic weights of the elements.

2. A formula is proposed for calculation of possible isotopes (excluding nuclear isomers) in a given portion of the periodic system, which provides the possibility of prediction of the number of isotopes discovered in recent years, thus confirming the view of D.I. Mendeleev that the difference in atomic weights may be a "tool" for "more detailed check of the experimental data".

3. The idealistic and agnostic conclusion of bourgeois science about the unknowability of the possible number of isotopes and about the lack of correlation of the number of isotopes with the periodic system of D. I. Mendeleev [11] is refuted.

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FUSION DIAGRAMS OF THE TERNARY SYSTEMS: POTASSIUM SULFATE — CHROMATE — NITRATE AND SODIUM SULFATE — CHROMATE — NITRATE

I. S. Rassonskaya and A. G. Bergman

The ternary systems $K\|SO_4, CrO_4, NO_3$ and $Na\|SO_4, CrO_4, NO_3$ are part of the quaternary reciprocal system of the sulfates, chromates and nitrates of sodium and potassium which has been studied in the Fused Salts Laboratory of the N. S. Kurnakov Institute of General and Inorganic Chemistry of the Academy of Sciences of the U.S.S.R.

The binary systems formed by nitrates and the corresponding sulfates or chromates are characterized, according to various authors, by the presence of a simple eutectic and by the absence of compounds and solid solutions:

K_2SO_4–$(KNO_3)_2$ [1,2];	eutectic 333°; 97.5%	$(KNO_3)_2$,
K_2CrO_4–$(KNO_3)_2$ [3];	eutectic 336°; 96.5%	$(KNO_3)_2$,
Na_2SO_4–$(NaNO_3)_2$ [2,4];	eutectic 330°; 90.5%	$(NaNO_3)_2$,
Na_2CrO_4–$(NaNO_3)_2$ [3];	eutectic 300°; 91%	$(NaNO_3)_2$.

Our own data (Table 1) are in agreement with the literature data [3].

TABLE 1 Na_2CrO_4–$(NaNO_3)_2$

% Na_2CrO_4	t°	% Na_2CrO_4	t°	% Na_2CrO_4	t°
0	308	8	302	20	390
3	308	9	300	25	412
5	308	10	316	30	456
6	307	12	332	35	485
7	304	15	360	45	542

Hence in the investigated ternary systems the low-melting nitrates function as solvents, nonreactive with the solid phases formed from the sulfates and chromates. Due to the depression of the crystallization temperature, the presence of such a solvent may lead to the appearance on the liquidus diagram of the ternary systems of fields of crystallization of those phases which, in the absence of a solvent, in the binary systems are formed only as a result of solid-state transformations [2,3,5].

K_2SO_4–K_2CrO_4 [6]. The phase diagram is plotted from cooling and heating curves. A continuous series of solid solutions crystallizes from the liquid melts of potassium sulfate and chromate. Between the temperatures of 585 and 666°, corresponding respectively to the polymorphic transformation of pure K_2SO_4 and K_2CrO_4, the α-solid solutions of the hexagonal modification undergo transformation with formation of β-solid solutions of the rhombic modification.

Na_2SO_4–Na_2CrO_4 [7]. The phase diagram was studied with the help of cooling curves of melts of various compositions. A liquidus curve with a very weakly defined minimum indicates the existence of a continuous series of solid solutions.

A transformation curve is also found in the solid state, starting from 235° on the side of pure Na_2SO_4 and from 413° on the side of pure Na_2CrO_4.

In view of the fact that the sulfate and chromate exist above the specified temperatures in the form of hexagonal modifications isomorphous with each other, while below those temperatures they exist as isomorphous rhombic modifications, the author in question [7] concludes that there are two forms of solid solutions of the high-temperature hexagonal α-modification and of the low-temperature rhombic β-modification.

Since in the ternary systems under discussion the nitrate is a low-melting solvent which does not form either compounds or solid solutions with the sulfate and chromate, we can observe the fields of crystallization of both the α- and the β-solid solutions at the liquidus surface in the sodium system. The appearance of crystallization fields of the two types of solid solutions should only occur with the potassium system if it were possible to conduct the determinations at temperatures above 585°.

The fusibility was studied by the visual-polythermal method in glass test tubes. Supercooling of the melts was avoided by stirring with a platinum stirrer. The temperature of appearance of the first crystals was measured

TABLE 2

Sections of the ternary system K_2SO_4–K_2CrO_4–$(KNO_3)_2$

I		II		III		IV		V		VI	
8% K_2CrO_4 92% $(KNO_3)_2$ → K_2SO_4		10% K_2CrO 90% $(KNO_3)_2$ → K_2SO_4		15% K_2CrO_4 85% $(KNO_3)_2$ → K_2SO_4		20% K_2CrO_4 80% $(KNO_3)_2$ → K_2SO_4		$(KNO_3)_2$ → → 30% K_2SO_4 70% K_2CrO_4		$(KNO_3)_2$ → → 60% K_2SO_4 40% K_2CrO_4	
% K_2SO_4	t°	% K_2SO_4	t°	% K_2SO_4	t°	% K_2SO_4	t°	% melt	t°	% melt	t°
0	398	0	450	0	500	0	531	0	337	0	337
1	410	1	463	1	504	1	534	1	337	1	337
2	420	2	470	2	510	2	538	2	336	2	336
3	436	3	477	3	516	3	540	3	332	3	332
4	450	4	482	4	520	4	544	4	339	4	350
5	460	5	496	5	528	5	550	5	363	5	374
6	474	6	500	6	535	6	554	6	386	6	397
7	489	7	511	7	540	7	558	8	420	8	431
8	500	8	518	8	545	8	565	10	449	10	459
9	507	10	530	9	551			13	480	12	478
10	513							15	499	14	498
11	521							18	517	16	518
12	531							20	529		
13	541										

TABLE 3

Temperatures of Start of Crystallization of Melts in the Ternary System Na_2SO_4–Na_2CrO_4–$(NaNO_3)_2$ at the Sections

I		II		III		IV	
$(NaNO_3)_2$ → 75% Na_2SO_4 25% Na_2CrO_4		$(NaNO_3)_2$ → 50% Na_2SO_4 50% Na_2CrO_4		$(NaNO_3)_2$ → 25% Na_2SO_4 75% Na_2CrO_4		$(NaNO_3)_2$ → 15% Na_2SO_4 85% Na_2CrO_4	
% melt	t°	% melt	t°	% melt	t°	% melt	t°
0	308	0	308	0	308	0	308
2	308	3	308	4	305	3	305
4	308	6	308	6	303	6	304
6	308	8	304	8	301	9	300
8	304	10	303	10	300	12	312
10	302	12	300	13	313	15	333
12	298	15	298	15	324	18	354
15	324	18	330	18	344	20	370
18	358	20	345	22	379	23	388
20	390	23	374	25	404	26	408
22	400	25	387	28	417	29	426
25	422	30	433	30	435	33	452
30	460			35	464		
34.8	486						

with the help of a nichrome-constantan thermocouple of 0.3 mm cross-section and a 17 mV galvanometer. The error in the temperature determination was 1-2°. The thermocouple was protected against the action of the melt by a glass sheath. The weight of the sample was 2.5-3 g. Successive points on the section were obtained by the method of addition.

The starting preparations were obtained by recrystallization of chemically pure grades of materials; sodium chromate was prepared from sodium bichromate or chromic oxide and sodium carbonate followed by recrystallization.

I. System K_2SO_4–K_2CrO_4–$(KNO_3)_2$. 6 sections of this system were investigated (Table 2).

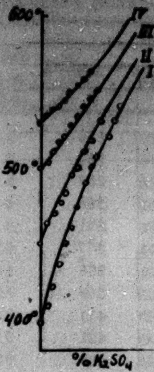

Fig. 1. Sections I to IV in the system K_2SO_4–K_2CrO_4–$(KNO_3)_2$.

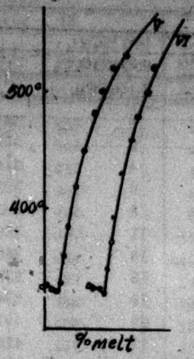

Fig. 2. Sections V and VI in the system K_2SO_4–K_2CrO_4–$(KNO_3)_2$.

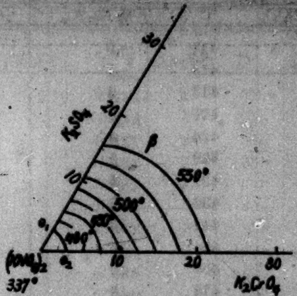

Fig. 3. Fusion diagram of the ternary system K ‖ SO_4, CrO_4, NO_3.

TABLE 3

V		VI		VII		VIII	
10% Na_2CrO_4 90% $(NaNO_3)_2$ $\rightarrow$	Na_2SO_4	12% Na_2CrO_4 88% $(NaNO_3)_2$ $\rightarrow$	Na_2SO_4	18% Na_2CrO_4 82% $(NaNO_3)_2$ $\rightarrow$	Na_2SO_4	21% Na_2CrO_4 79% $(NaNO_3)_2$ $\rightarrow$	Na_2SO_4
% Na_2SO_4	t°	% Na_2SO_4	t°	% Na_2SO_4	t°	% Na_2SO_4	t°
0	306	0	323	0	366	0	391
1	306	1	323	1	366	1	391
3	307	2	323	2	366	2	391
5	307	3	323	3	366	3	391
6	307	4	323	4	366	4	396
7	316	5	323	5	371	5	400
8	327	6	323	6	376	6	405
9	333	7	330	7	380	7	410
10	344	8	340	8	386	8	416
11	360	10	360	9	393	9	423
13	380	13	388	11	405	11	435
15	400	15	406	13	418	13	445
18	429	18	429	14	425	14	450
20	446	20	445	16	441	17	468
23	470	23	470	18	457	18	480
28	505	26	491	20	487		

Corresponding to the first four sections is only one crystallization branch, relating to the separation of solid solutions of potassium sulfate and chromate (Fig. 1). On the radial sections issuing from the nitrate corner are two well-defined branches corresponding to the crystallization of nitrate and chromate-sulfate solid solutions (Fig. 2). The liquidus surface of the ternary system, represented in Fig. 3, consists of two fields corresponding to the crystallization of potassium nitrate and solid solutions of potassium sulfate and chromate.

The presence of potassium nitrate, which decomposes at 520-550° [8], prevented study of the fusibility at higher temperatures; consequently the solid solutions crystallizing in the investigated region consist of the β-modification which exists at below 585° [6]. The line of joint separation of potassium nitrate and the β-solid solutions has a minimum at 330° and the composition of 96% $(KNO_3)_2$ + 2% K_2SO_4 + 2% K_2CrO_4.

TABLE 3 (Continuation)

IX		X		XI		XII	
25% Na_2CrO_4 75% $(NaNO_3)_2$ → Na_2SO_4		29% Na_2CrO_4 71% $(NaNO_3)_2$ → Na_2SO_4		10% Na_2SO_4 90% $(NaNO_3)_2$ → Na_2CrO_4		13% Na_2SO_4 87% $(NaNO_3)_2$ → Na_2CrO_4	
% Na_2SO_4	t°	% Na_2SO_4	t°	% Na_2CrO_4	t°	% Na_2CrO_4	t°
0	412	0	442	0	304	0	350
1	414	1	445	2	309	2	354
2	416	2	447	4	314	4	358
3	420	3	449	6	323	6	365
4	424	4	451	8	332	8	371
5	428	5	453	11	350	10	377
6	431	6	457	13	365	12	386
7	436	8	462	15	378	14	398
9	447	10	467	18	394	16	411
11	454	13	478	20	407	18	421
13	464	15	484	22	422	20	435
15	478	18	498	24	435	22	446
20	495			27	448	24	457
				29	460	26	467

II. System Na_2SO_4-Na_2CrO_4-$(NaNO_3)_2$. 15 sections were investigated in the course of the study of this system. (Table 3).

On the first two sections (Figure 4) two branches are clearly visible, corresponding to the crystallization of $NaNO_3$ and of solid solutions of Na_2SO_4-Na_2CrO_4. Section III (Figure 5) has three branches, two of which, evidently belonging to the two types of solid solutions, intersect at a very obtuse angle. The crystals corresponding to these branches differ in outward appearance, which fact may serve as confirmation of the presence of different solid phases. Two branches appear on section IV (Figure 5); after the 8th point, however, the outward appearance of the crystals changes appreciably and becomes the same as that of the crystals separating in sections I, II and III. Evidently, section IV, like section III, must consist not of two branches but of three. In sections V to VIII (Figure 6) there are two very well developed branches corresponding to crystals with differing forms – the two types of solid solutions. The second branches of sections V, VII, VIII (Figure 6), XI, XII and XIII (Figure 7) are initially slightly concave but subsequently become rectilinear. In the opinion of A. G. Bergman, sections V, VII and VIII consist of three branches, two of which form very obtuse intersection angles. Bergman therefore concludes that there is a field of crystallization of some other new solid phase. The sections from IX to XV are characterized by the presence of one regularly rising curve with a weak concavity corresponding to the crystallization of solid solutions of sodium sulfate and chromate.

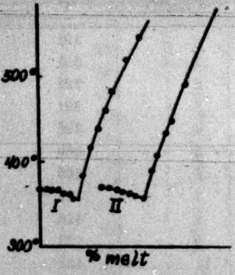

Figure 4 Sections I and II in the System Na_2SO_4-Na_2CrO_4-$(NaNO_3)_2$.

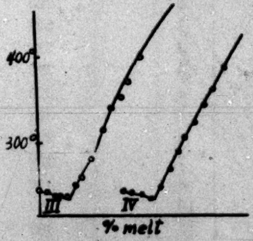

Figure 5. Sections III and IV in the system Na_2SO_4-Na_2CrO_4-$(NaNO_3)_2$.

No difference between the crystals of the solid phases separating throughout the whole extent of the section is detectable by the naked eye.

TABLE 3 (Continuation)

XIII		XIV		XV	
16% Na_2SO_4 84% $(NaNO_3)_2$ → Na_2CrO_4		19% Na_2SO_4 81% $(NaNO_3)_2$ → Na_2CrO_4		22% Na_2SO_4 78% $(NaNO_3)_2$ → Na_2CrO_4	
% Na_2CrO_4	t°	% Na_2CrO_4	t°	% Na_2CrO_4	t°
0	381	0	417	0	451
2	386	2	418	2	454
4	391	4	419	4	456
6	396	6	421	6	459
8	401	8	426	8	461
10	406	10	429	10	464
12	413	12	434	12	466
14	421	14	439	14	472
16	431	16	445	16	477
18	441	18	450	18	483
20	450	20	457	20	489
23	466	22	466	22	495
26	479	24	476		
29	498	26	486		

On the basis of the investigated sections, the fusion diagram of the ternary system Na_2SO_4–Na_2CrO_4–$(NaNO_3)_2$ was plotted (Figure 8). There is no doubt about the existence of three fields of crystallization: an extremely small field corresponding to the crystallization of sodium nitrate; a large field corresponding to the separation of α-solid solutions of sodium sulfate and chromate; and a small field adjacent to the Na_2CrO_4–$NaNO_3$ side corresponding apparently to the crystallization of the β-modification of the solid solutions of sodium sulfate and chromate. The broken curve marks the boundary of the internal field mentioned by A. G. Bergmann, corresponding to the crystallization of some new phase.

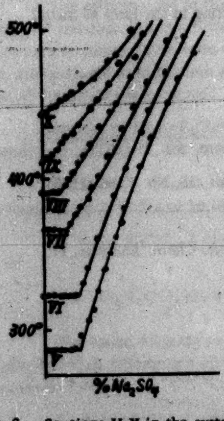

Figure 6. Sections V-X in the system Na_2SO_4–Na_2CrO_4–$(NaNO_3)_2$.

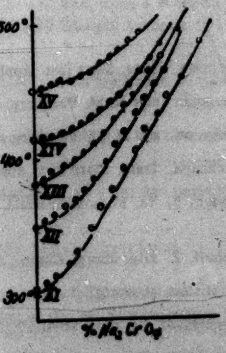

Figure 7. Sections XI-XV in the system Na_2SO_4–Na_2CrO_4–$(NaNO_3)_2$.

In order to determine the crystallization fields of the various solid phases, however, it is not always sufficient to study only the liquidus surface; in some cases it is necessary also to study the solid phases themselves. We attempted to clarify the problem to some extent by an investigation of these melts with the help of heating and cooling curves, using a differential recording device on N. S. Kurnakov's pyrometer. The temperatures of transformation of the pure salts that we found were: 241° for Na_2SO_4, 413° for Na_2CrO_4, and 276° for $NaNO_3$.

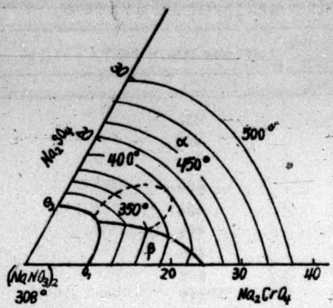

Figure 8. Fusion diagram of the ternary system Na || SO_4, CrO_4, NO_3

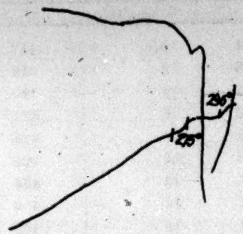

Figure 9. Heating curve of the melt: 73% $(NaNO_3)_2$ + 17% Na_2SO_4 + 10% Na_2CrO_4.

which were in good agreement with the literature values. The same may be said about the transformation temperatures in the solid solutions of the binary system of sodium sulfate and chromate. However, in repeated attempts to study the ternary melts by the method of heating and cooling curves, (Figure 9) we only detected the effects of transformation of sodium nitrate and of conjoint fusion of mixtures of nitrate with sulfate-chromate solid solution. The effect of transformation of the solid solutions of Na_2SO_4-Na_2CrO_4 evidently overlaps with that of the effects of transformation of sodium nitrate and of the joint fusion of sodium nitrate with the solid solution of Na_2SO_4-Na_2CrO_4. Due to the fact that the decomposability of sodium nitrate prevented investigation of melts other than those with a relatively low temperature of separation of the initial crystals, which are close to the nitrate corner [73-85% $(NaNO_3)_2$], it is understandable that the effects of transformation of nitrate and joint fusion of mixtures of nitrate with solid solutions of Na_2SO_4-Na_2CrO_4 must greatly predominate over all other effects, since there is a large proportion of nitrate in the melt but very little of the solid solutions separating in the form of initial crystals.

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THE DIAGONAL SECTIONS OF THE QUATERNARY RECIPROCAL SYSTEM OF THE FLUORIDES, CHLORIDES AND CHROMATES OF SODIUM AND POTASSIUM

N. S. Rassonskaya and A. G. Bergman

Further data on the quaternary reciprocal system Na, K$\|$F, Cl, CrO_4 are presented in this paper. Studies were previously made of the fusion diagrams of the ternary systems K$\|$F, Cl, CrO_4 and Na$\|$F, Cl, CrO_4 [1] on the basis of the prism shown in Figure 1. The ternary reciprocal system Na, K$\|$F, Cl has been investigated by Polyakov [2].

Double decompositions at the lateral faces of the prism of the reciprocal systems take place, according to the following equations, with the thermal effects indicated [3]:

$K_2F_2 + Na_2CrO_4 \rightarrow Na_2F_2 + K_2CrO_4$ + 8.24 kcal per equiv.
269.02 319.8 271.90 333.40

$K_2Cl_2 + Na_2CrO_4 \rightarrow Na_2Cl_2 + K_2CrO_4$ + 0.96 kcal per equiv.
208.34 319.8 196.66 333.40

$KF + NaCl \rightarrow NaF + KCl$ + 7.28 kcal per equiv.
134.51 98.33 135.95 104.17

The most stable diagonal is Na_2F_2–K_2CrO_4, whose thermal effect is equal to the sum of the thermal effects of the two other diagonals: 8.24 = 0.96 + 7.28.

Melts of the investigated quaternary reciprocal system possess, apart from general importance, practical interest as salt baths.

The salts utilized in the investigation were chemically pure grades which were recrystallized, then dried at 120° and calcined in a furnace at 500°. Temperatures of appearance and disappearance of crystals in melts of various compositions were determined visually in a platinum crucible, using a Pt-Rh-Au-Pt-Pd thermocouple with a diameter of 0.3 mm and a 17 mV galvanometer. The readings were accurate to 1-2°. Supercooling of the melts was prevented by using a platinum stirrer.

Section of Na_2F_2–K_2Cl_2–K_2CrO_4 (Figure 1). Two sides of this section are stable diagonals in the ternary reciprocal systems.

1. NaF–KCl, diagonal in the system Na, K$\|$F, Cl, possesses according to our data (Table 1) an inflection-eutectic point at 652° and 26.5% NaF.

2. Na_2F_2–K_2CrO_4, a diagonal in the system Na, K$\|$F, CrO_4, has an inflection point at 30% Na_2F_2 and 730°.

3. K_2Cl_2–K_2CrO_4 has been studied by S. F. Zhemchuzhny [4] and again by us.

The fusion diagram contains a eutectic point at 650° and 52% K_2Cl_2 and an inflection at 666° and 50% K_2Cl_2 at which intersection occurs of the crystallization branches of the two heteromorphic modifications of potassium chromate.

Fusibility in the diagonal section Na_2F_2–K_2Cl_2–K_2CrO_4 was studied along six cuts (Table 1, Figures 2 and 3).

The curves corresponding to the crystallization of NaF, K_2CrO_4 and KCl intersect at an acute angle. The branches corresponding to the separation of the α- and β-modifications of potassium chromate in some cases exhibit very slight breaks. Their detection and the establishment of the composition at the intersection points necessitated the determination of the temperature of separation of crystals from melts whose compositions differed by 1-2% of added salt.

TABLE 1

Cuts in the Diagonal Section of $Na_2F_2-K_2Cl_2-K_2CrO_4$ in the Quaternary Reciprocal System Na, K‖F, CrO_4 (in mole-%)

No.	Side NaF–KCl		Cut 1 $\left.\begin{matrix}20\% K_2CrO_4\\80\% K_2Cl_2\end{matrix}\right\}\rightarrow Na_2F_2$		Cut 2 $\left.\begin{matrix}35\% K_2CrO_4\\65\% K_2Cl_2\end{matrix}\right\}\rightarrow Na_2F_2$		Cut 3 $\left.\begin{matrix}60\% K_2CrO_4\\40\% K_2Cl_2\end{matrix}\right\}\rightarrow Na_2F_2$		Cut 4 $\left.\begin{matrix}20\% Na_2F_2\\80\% K_2Cl_2\end{matrix}\right\}\rightarrow K_2CrO_4$	
	%NaF	t°	$\%Na_2F_2$	t°	$\%Na_2F_2$	t°	$\%Na_2F_2$	t°	$\%K_2CrO_4$	t°
1	0	773	0	730	0	691	0	706	0	678
2	5	748	5	704	5	666	5	680	5	670
3	10	724	10	682	10	642	10	655	10	663
4	15	700	15	659	15	623	15	631	15	656
5	20	680	20	639	20	602	20	620	20	647
6	25	661	25	646	25	627	25	656	25	639
7	30	674	30	673	30	666	30	686	30	630
8	35	703	35	696	35	697	35	710	35	620
9	40	730	40	720	40	724	40	734	40	605
10	45	753	45	747	45	752	45	758	45	613
11	100	990	50	770	100	990	50	780	50	636
12			55	790			55	802	55	666
13			60	812			100	990	60	696
14			65	836					65	734
15			70	860					100	984
16			100	990						
17										

The constancy of the transformation temperature of the α- and β-modifications of K_2CrO_4 (666°) is evidence of the absence of solid solutions.

Consequently, judging by the character of the liquidus surface (Figure 4) the section $Na_2F_2-K_2Cl_2-K_2CrO_4$ must be classed as a stable section since the fusion diagram only contains fields of crystallization corresponding to the components forming this section: NaF, KCl, and K_2CrO_4. The field of crystallization of potassium chromate on the 666° isotherm is divided into two surfaces corresponding to its two modifications.

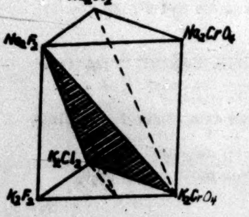

Figure 1. Distribution of sections in the prism of the quaternary reciprocal system Na, K‖F, Cl, CrO_4.

The fusion diagram of this stable diagonal section contains one ternary eutectic point and one inflection point.

The fields of KCl, NaF and β-K_2CrO_4 meet at the ternary eutectic; the latter corresponds to 44% K_2Cl_2 + 16% Na_2F_2 + 40% K_2CrO_4 and 580°.

The inflection point corresponds to 666° and the composition 16% K_2Cl_2 + 24% Na_2F_2 + 60% K_2CrO_4. This point is the juncture of the surfaces of crystallization of NaF, α-K_2CrO_4 and β-K_2CrO_4.

Section $Na_2F_2-Na_2Cl_2-K_2CrO_4$ (Figure 1). The sides of this section are: the binary system $Na_2F_2-Na_2Cl_2$ and the diagonals $Na_2F_2-K_2CrO_4$ and $Na_2Cl_2-K_2CrO_4$ in the ternary reciprocal systems Na, K‖F, CrO_4 and Na, K‖Cl, CrO_4.

The fusion diagram of the system NaF–NaCl consists of two curves intersecting at the eutectic point corresponding to 674° and 33% NaF.

The polytherm of the system $Na_2Cl_2-K_2CrO_4$ consists of five branches corresponding to the crystallization of α- and β-K_2CrO_4, chromglaserite ($3K_2CrO_4 \cdot Na_2CrO_4$), KCl and NaCl. The KCl crystallization branch is very short. The point of intersection with the diagonal of the line of joint crystallization of K_2CrO_4 and chromglaserite corresponds to 592° and 37.5% Na_2Cl_2.

The points of intersection with the diagonal of the lines of joint separation of chromglaserite with KCl and of KCl with NaCl correspond respectively to 540 and 536° and the compositions 47.5% Na_2Cl_2 and 53% Na_2Cl_2.

TABLE 1

Cuts in the Diagonal Section of $Na_2F_2-K_2Cl_2-K_2CrO_4$ in the Quaternary Reciprocal System Na, K F, CrO_4 (in mole-%)

Cut 5		Cut 6	
33% Na_2F_2 + 67% K_2Cl_2 → K_2CrO_4		25% Na_2F_2 + 75% K_2CrO_4 → K_2Cl_2	
% K_2CrO_4	t°	% K_2Cl_2	t°
40	603	0	770
42	602	10	722
44	602	20	679
46	605	22	673
48	612	24	665
50	628	26	659
52	636	28	654
53	642	30	647
54	649	33	636
55	656	36	624
57	666	39	613
60	687	42	600
65	720	45	598
100	984	48	609
		50	615
		55	634
		100	773

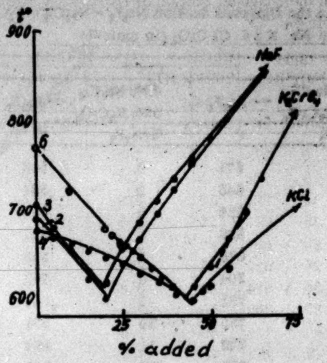

Figure 2. Cuts 2,3,4,6 in the diagonal section $Na_2F_2-K_2Cl_2-K_2CrO_4$.

Fusibility in the diagonal section $Na_2F_2-Na_2Cl_2-K_2CrO_4$ was examined along with five cuts (Table 2, Figures 5 and 6).

The polytherms of the first four cuts have two branches, one of which corresponds to the crystallization of NaF. The second crystallizing phase (in the order of the cuts) will be: β-K_2CrO_4, chromglaserite, KCl and NaCl; the fifth cut, extending from the NaF-NaCl side to the K_2CrO_4 apex, has five branches corresponding to the crystallization of NaCl, KCl, chromglaserite, β-K_2CrO_4 and α-K_2CrO_4.

The crystallization surface obtained on the basis of the investigated cuts is represented in Figure 7. The greater part is occupied by the field corresponding to the separation of NaF.

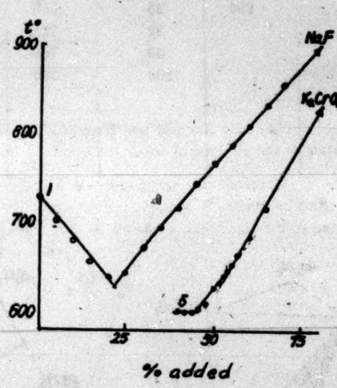

Figure 3. Cuts 1 and 5 in the diagonal section $Na_2F_2-K_2Cl_2-K_2CrO_4$.

The diagonal section $Na_2F_2-Na_2Cl_2-K_2CrO_4$ is unstable since the liquidus surface consists of six fields corresponding to crystallization of the three components of this section (NaF, NaCl and K_2CrO_4 in its two modifications) and the products of double decomposition (KCl and chromglaserite).

In the unstable section are the points A, B, C and D of common phase separation:

At point A, corresponding to 666° and 66% K_2CrO_4 + 20% Na_2F_2 + 14% Na_2Cl_2, simultaneous crystallization occurs of α-K_2CrO_4, β-K_2CrO_4 and NaF.

At point B, corresponding to 564° and 58% K_2CrO_4 + 5% Na_2F_2 + 37% Na_2Cl_2, crystallization takes place of NaF, β-K_2CrO_4 and chromglaserite.

At point C, corresponding to 526° and 47% K_2CrO_4 + 8% Na_2F_2 + 45% Na_2Cl_2, simultaneous separation of NaF, KCl and chromglaserite occurs.

At point D, corresponding to 528° and 45% K_2CrO_4 + 6% Na_2F_2 + 49% Na_2Cl_2, there is joint crystallization of NaF, NaCl and KCl. Low-melting melts of both of the sections: 1) 44% K_2Cl_2 + 16% Na_2F_2 + 40% K_2CrO_4

TABLE 2

Cuts in the Diagonal Section $Na_2F_2 - Na_2Cl_2 - K_2CrO_4$ of the Quaternary Reciprocal System Na, K ‖ F, Cl, CrO_4 (in mole-%)

Cut 1		Cut 2		Cut 3		Cut 4		Cut 5	
30% Na_2Cl_2 70% K_2CrO_4 $\rightarrow Na_2F_2$		43% Na_2Cl_2 57% K_2CrO_4 $\rightarrow Na_2F_2$		50% Na_2Cl_2 50% K_2CrO_4 $\rightarrow Na_2F_2$		60% Na_2Cl_2 40% K_2CrO_4 $\rightarrow Na_2F_2$		10% Na_2F_2 90% Na_2Cl_2 $\rightarrow K_2CrO_4$	
% Na_2F_2	t°	% Na_2F_2	t°	% Na_2F_2	t°	% Na_2F_2	t°	% K_2CrO_4	t°
0	671	0	566	0	532	0	585	0	767
5	645	3	564	1	531	5	570	10	712
10	626	5	560	2	530	10	554	20	659
15	636	6	557	3	529	15	598	30	602
20	676	7	555	4	529	20	636	35	573
25	704	8	552	5	528	25	682	40	552
30	731	9	560	6	525	30	713	42	543
35	753	10	571	7	524	35	738	44	534
40	772	11	584	8	533	40	764	45	528
45	792	12	593	9	546	45	786	46	528
50	817	15	623	10	557	50	812	47	528
55	838	20	660	13	585	60	845	48	528
100	990	25	695	15	616	100	990	49	528
		30	723	20	658			50	538
		40	768	25	692			55	567
		100	990	30	722			60	586
				35	749			65	637
				45	804			70	680
				100	990			75	728
								100	984

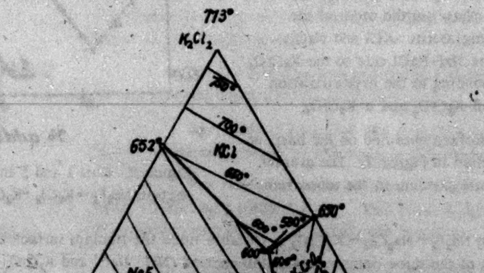
773°
K_2Cl_2
750°
700°
KCl
652°
650°
650°
600
580°
600°
β-K_2CrO_4
650°
700°
750°
NaF
650°
700°
α-K_2CrO_4
800°
850°
900°
950°
850°
900°
750°
800°
950
730°
Na_2F_2
990°
K_2CrO_4
984°

Figure 4. Liquidus surface of the diagonal section Na_2F_2–K_2Cl_2–K_2CrO_4

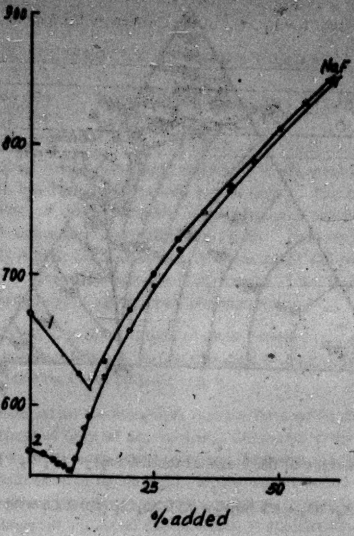

Figure 5 Cuts 1 and 2 in the diagonal section $Na_2F_2-Na_2Cl_2-K_2CrO_4$.

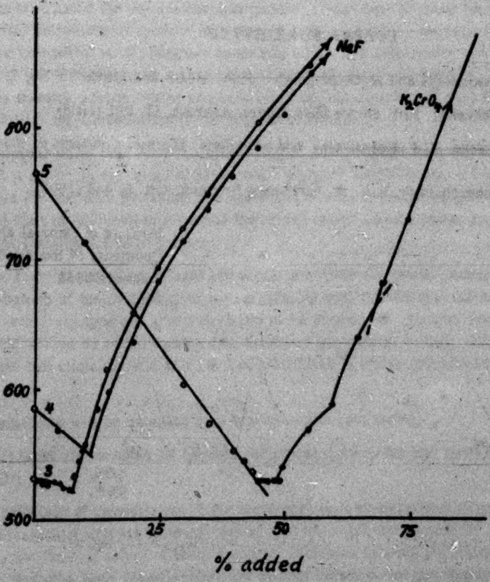

Figure 6. Cuts, 3, 4, 5 in the diagonal section $Na_2F_2-Na_2Cl_2-K_2CrO_4$

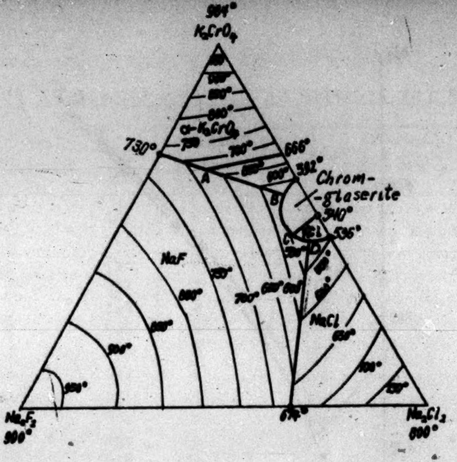
984°
K_2CrO_4
α-K_2CrO_4
730°
750°
700°
666°
592°
Chrom-
-glaserite
540°
536°
A
B
C
D
NaCl
NaF
750°
800°
850°
900°
950°
700°
NaCl
Na_2F_2
900°
674°
Na_2Cl_2
800°

Figure 7. Liquidus surface of the diagonal section $Na_2F_2 - Na_2Cl_2 - K_2CrO_4$.

with melting point 580° and 2) 47% K_2CrO_4 + 8% Na_2F_2 + 45% Na_2Cl_2 (point C) with melting point 526° are of interest as salt baths.

The investigated quaternary reciprocal system is an analog of the system Na, K ‖ F, Cl, SO_4. Comparison of these systems permits clarification of the effect of replacement of the chromate ion by the sulfate ion on complex formation and on the shift of the double decomposition reactions.

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CLASSIFICATION OF THE RECIPROCAL SYSTEMS FORMED BY THE ALKALI METALS

G. G. Diogenov

About 200 reciprocal systems have been studied up to the present time. The investigation, as A. G. Bergman [1] has pointed out, has involved 25 cations and 30 anions. This is an enormous project, but it includes a relatively small proportion of the total number of metals (about one third) and by no means all the known anions. We are confronted with a great and intricate problem: To investigate nearly 50 cations and more than 10 anions. Particularly serious difficulties will be encountered and (we must hope) interesting results will be obtained in a study of the reciprocal systems involving cations of the eighth group, also cations of the rare-earth elements and of some subgroups of Mendeleev's periodic system.

We can justifiably say that the inclusion of these cations in the project will enrich chemistry not only by the discovery of new compounds but by the clarification of many problems relating to the nature of these cations and to their special position in the periodic system.

The wealth of material on the reciprocal systems obtained by the researches of a large group, centered mainly in the Institute of General and Inorganic Chemistry of the Academy of Sciences of the USSR (Moscow) but also operating in other towns (Rostov-on-Don, Voronezh, Irkutsk) enabled A. G. Bergman as far back as 1929 to set about classification of the data [2]; in this research A. G. Bergman and N. S. Dombrovskaya divided all the reciprocal systems into three types: reversible-reciprocal, irreversible-reciprocal, irreversible reciprical systems with a pronounced unilateral displacement of equilibrium (singular systems). This classification was correlated with the different thermal effects in double decompositions: For the first type the thermal effect is up to 2 kcal; for the second type it is 2 to 10 kcal; for the third type it is over 10 kcal.

The basis of this classification – the thermal effect of the reversible reaction – proved to be generally valid and has facilitated the correct characterization of the type of many reciprocal systems. But the accumulation of material on reciprocal systems with sharply defined complex formation and also with solid solutions and polymorphism compelled A. G. Bergman to greatly widen and supplement the original classification. In his latest publications [4] A. G. Bergman introduces new types of reciprocal systems: diagonal, adiagonal, mixed, rectangular and transition types, whose characteristics are correlated both with the thermal effect of the reversible reaction and with the triangulation of the reciprocal systems.

Experiment shows that even this broadening of classification does not embrace all types of ternary reciprocal systems, and it is not, in our opinion, definitive. We must conclude that a broader classification of reciprocal systems will be created only by taking into account the position of the cations in Mendeleev's periodic system, i.e., we should start on the basis of a natural law which knows no exceptions and is the preeminent instrument for gaining insight into the nature of matter.

In the study of the alkali nitrate and alkali chromate reciprocal systems with participation of cations of the main subgroup of the first group of the periodic system, the thermal effect of these reactions, arranged in a definite order, engaged our attention owing to its periodicity. Further investigations showed that all other reciprocal systems formed by alkali cations also exhibited periodicity in their thermal effects. This observation prompted us to take this characteristic as a basis of classification of reciprocal systems formed with alkali metals.

Our approach will be clarified by a few examples (see table).

In this table are included 10 possible reciprocal systems for four pairs of anions ($OH'-NO_3'$, $OH'-Cl'$, $OH'-CO_3''$, $F'-Cl'$).

The principle of arrangement of the reciprocal systems according to groups has the following basis. In the first group are included all those reciprocal systems which are formed by adjacent alkali metals. As we see from the table, the thermal effect of these reactions decreases in a regular manner. In the second group of reciprocal systems are included those systems which are formed by alkali metals separated by one other element in the periodic system. The thermal effect of these systems also regularly declines from top to bottom. In the third group of reciprocal systems are brought those systems containing alkali metals separated from one another in the periodic table by two elements. Their thermal effect (in passage from top to bottom) also regularly falls. The fourth group contains the first alkali metal (lithium) and the last one in the periodic table (cesium). Here the thermal effect is at a maximum.

The fall in thermal effect is a feature of all the groups. The first systems in the groups exhibit the most pronounced displacement of equilibrium; this gradually diminishes and reaches its lowest value in the bottom of the groups.

On comparing the horizontal series of the table, we see that the thermal effect of the respective reciprocal systems continuously increases from the first group to the last. At the start of the series are reciprocal systems with the smallest displacement of equilibrium and there is a gradual increase to a maximum in the last series.

TABLE

	Reciprocal systems							
	1st group		2nd group		3rd group		4th group	
series	system	thermal effect (in kcal)	system	thermal effect (in kcal)	system	thermal effect (in kcal)	system	thermal effect (in kcal)
1	$Li, Na \| OH, NO_3$	11.2	$Li, K \| OH, NO_3$	17.3	$Li, Rb \| OH, NO_3$	19.1	$Li, Cs \| OH, NO_3$	22.0
2	$Na, K \| OH, NO_3$	6.1	$Na, Rb \| OH, NO_3$	7.9	$Na, Cs \| OH, NO_3$	10.8	–	–
3	$K, Rb \| OH, NO_3$	2.0	$K, Cs \| OH, NO_3$	4.7	–	–	–	–
4	$Rb, Cs \| OH, NO_3$	3.0	–	–	–	–	–	–
1	$Li, Na \| OH, Cl$	15.4	$Li, K \| OH, Cl$	21.0	$Li, Rb \| OH, Cl$	22.7	$Li, Cs \| OH, Cl$	25.1
2	$Na, K \| OH, Cl$	5.7	$Na, Rb \| OH, Cl$	7.3	$Na, Cs \| OH, Cl$	9.7	–	–
3	$K, Rb \| OH, Cl$	1.6	$K, Cs \| OH, Cl$	4.0	–	–	–	–
4	$Rb, Cs \| OH, Cl$	2.4	–	–	–	–	–	–
1	$Li, Na \| OH, CO_3$	4.3	$Li, K \| OH, CO_3$	6.4	$Li, Rb \| OH, CO_3$	6.8	$Li, Cs \| OH, CO_3$	7.1
2	$Na, K \| OH, CO_3$	2.1	$Na, Rb \| OH, CO_3$	2.5	$Na, Cs \| OH, CO_3$	2.8	–	–
3	$K, Rb \| OH, CO_3$	0.4	$K, Cs \| OH, CO_3$	0.7	–	–	–	–
4	$Rb, Cs \| OH, CO_3$	0.3	–	–	–	–	–	–
1	$Li, Na \| F, Cl$	10.2	$Li, K \| F, Cl.$	18.4	$Li, Rb \| F, Cl$	19.9	$Li, Cs \| F, Cl$	22.6
2	$Na, K \| F, Cl$	8.2	$Na, Rb \| F, Cl$	9.7	$Na, Cs \| F, Cl$	12.4	–	–
3	$K, Rb \| F, Cl$	1.5	$K, Cs \| F, Cl$	4.2	–	–	–	–
4	$Rb, Cs \| F, Cl$	2.7	–	–	–	–	–	–

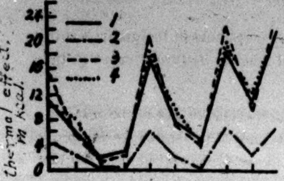
Consequently, in passing from one group of reciprocal systems to another we observe that the thermal effect regularly falls in the first group, then sharply rises in the second group, then gradually falls, and once again sharply rises at the start of the third group, and finally again falls and sharply rises in the fourth group.

Thus the thermal effect of reciprocal systems formed by the alkali metals changes periodically within the framework of the Mendeleev periodic group, as is clearly illustrated in Figure 1.

The foregoing considerations permit a new approach to the problem of classification of reciprocal systems. The reciprocal systems possible for the alkali metals are divided into ten types, the type of the system being determined by its place in the table. For example, a system formed from lithium and sodium, independently of the anions, will always be located in the first group and first series and is, as a rule, an irreversible system. Systems formed from sodium and rubidium must go into the second group and second series of reciprocal systems. Systems of this type will most usually be irreversible-reciprocal and their equilibrium shift (for a given pair of anions) will be greater than in systems belonging to the first group and second series of reciprocal systems.

The chief advantage of this classification is that it is closely linked to the periodic system of the elements and supplies an unequivocal answer to the question: What is the character of a given system and how is it related to reciprocal systems of other pairs of alkali metals (for a given pair of anions)?

Utilization of the proposed classification enables the effect of anions on the equilibrium shift in reciprocal systems to be more easily explained. It is clear from the table, in fact, that reciprocal systems of one type (systems occupying one and the same position in the classification table) with identical cations and a common ion (in our case hydroxyl) have a considerably greater shift of equilibrium in the case of the Cl' ion (radius 1.81 A), a rather smaller shift if the second anion is NO_3' (radius 2.36A), and a quite insignificant equilibrium shift when the CO_3'' ion (radius 2.57A) is present. This regular change in equilibrium shift in the systems appears to us to be in direct correlation with the magnitude of the ionic radius. The equilibrium shift is greater in systems (other conditions being equal) in which the anion has a smaller radius.



Change of thermal effect of double decomposition in reciprocal systems formed by the alkali metals.

Systems: 1) alkali nitrate, 2) alkali carbonate, 30alkali chloride, 4) chloride fluoride.

The proposed classification is valid in our opinion for reciprocal systems formed by metals of one group and does not embrace reciprocal systems formed by metals of different groups of the periodic system. But this fact by no means implies the incorrectness of our considerations; rather does it show that we have succeeded in dealing with only part of the complex and interesting problem. Other research work, possibly on a larger scale, on the classification of reciprocal systems awaits fresh investigators and the accumulation of supplementary experimental material.

SUMMARY

1. The thermal effect of reciprocal systems formed by the alkali metals varies periodically within the limits of the groups of the Mendeleev system.

2. The reciprocal systems possible for alkali metals are classified into ten types, the type of system being determined by its position in a table compiled on the basis of the distance between the alkali metals in the periodic system.

3. Equilibrium in the reciprocal systems is displaced the more strongly the smaller the radius of the anion (with an identical pair of cations and a common anion – in our case hydroxyl).

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CHARACTERISTIC PROPERTIES OF ALKALI HYDROXIDE-NITRATE SYSTEMS

G. G. Diogenov

The systematic study of reciprocal systems of one exchange decomposition enables the observation of certain regularities characterizing the given reciprocal systems and underlining their difference from systems of another exchange decomposition. In particular, systematic studies permit the establishment of preliminary statements about the specific properties of the anions undergoing transformations in the systems. For example, it is very probably correct to say that the OH' ion always increases the numer of compounds in systems, while the NO_3' ion very often leads to stratification. The F', Cl' Br' and I' ions generally form systems with a small number of compounds and the thermal effect of these reactions (for a given pair of cations) changes periodically within a given group of the periodic system of Mendeleev. More singular systems are formed by nonmetals separated in Mendeleev's periodic system by one or two elements; systems with a smaller equilibrium shift are always formed by nonmetals arranged in Mendeleev's table side by side. The foregoing observations are well illustrated by Table 1 and Figure 1.

TABLE 1

Exchange decomposition	Series	First group		Second group		Third group	
		Reciprocal systems					
		Systems	Thermal effect	Systems	Thermal effect	Systems	Thermal effect
Lithium-sodium	1	Li, Na ‖ F, Cl	10.2	Li, Na ‖ F, Br	12.59	Li, Na ‖ F, I	13.82
	2	Li, Na ‖ Cl, Br	2.29	Li, Na ‖ Cl, I	3.52		
	3	Li, Na ‖ Br, I	1.23				
Lithium-cesium	1	Li, Cs ‖ F, Cl	22.6	Li, Cs ‖ F, Br	27.78	Li, Cs ‖ F, I	32.71
	2	Li, Cs ‖ Cl, Br	5.22	Li, Cs ‖ Cl, I	10.15		
	3	Li, Cs ‖ Br, I	4.93				

Similar regularities are exhibited in other halide exchanges; but although halide exchange is interesting in many respects, it is not the main subject of our discussion. In the present paper we wish to consider rather more closely the alkali hydroxide-nitrate exchange decomposition, which attracts our interest both from the theoretical aspect (ortho salts, stratification, periodicity) and from the practical aspect since many melts of the reciprocal systems of this exchange can be recommended as heat transfer media.

We present the most important properties of the reciprocal systems of alkali hydroxides and nitrates in a table and we then discuss the data. The 10 possible systems of alkali hydroxides and nitrates are listed in Table 2. In the first group of this table are arranged the reciprocal systems formed by alkali metals occurring side by side in Mendeleev's periodic system. Their thermal effect (within the group), and consequently also the degree of shift of equilibrium, decreases in passage from top to bottom. The second group contains reciprocal systems formed by alkali metals which are separated from one another by one element in the periodic system. Their thermal effect, and consequently the degree of shift of equilibrium, (within the group), likewise decreases as we pass from top to bottom.

In the third group are reciprocal systems formed by alkali metals separated from one another in the periodic system by two elements. The thermal effect of these reversible reactions and the equilibrium shift (from top to bottom) also regularly decrease. The fourth group contains the reciprocal system formed by the first metal in the series (lithium) and the last metal (cesium). Its thermal effect and the degree of equilibrium shift are at a maximum. We thus see that the thermal effect of reciprocal systems formed by the alkali metals changes periodically within the first group of the Mendeleev system.

Stable pairs in all the reciprocal systems are formed by the alkalis with lower molecular weight and nitrates with higher molecular weight (and, as a rule, with higher melting point, except in the system K, Rb ‖ OH, NO_3,

TABLE 2

Groups	Series	Systems	Thermal effect (in kcal)	Stable pair	Stratification	Notes
I	1	Li, Na ‖ OH, NO_3	11.2	LiOH–$NaNO_3$	No	System studied by G. G. Diogenov
	2	Na, K ‖ OH, NO_3	6.1	NaOH–KNO_3	No	System studied by N. A. Reshetnikov
	3	K, Rb ‖ OH, NO_3	2.0	KOH–$RbNO_3$	No	Not investigated
	4	Rb, Cs ‖ OH, NO_3	3.0	RbOH–$CsNO_3$	No	Not investigated
II	1	Li, K ‖ OH, NO_3	17.3	LiOH–KNO_3	Yes	System studied by G. G. Diogenov
	2	Na, Rb ‖ OH, NO_3	7.9	NaOH–$RbNO_3$	Yes	Stable diagonal investigated by G.G.Diogenov (Figure 2)
	3	K, Cs ‖ OH, NO_3	4.7	KOH–$CsNO_3$	Yes	Not investigated
III	1	Li, Rb ‖ OH, NO_3	19.1	LiOH–$RbNO_3$	Yes	Stable diagonal investigated by G.G. Diogenov (Figure 2)
	2	Na, Cs ‖ OH, NO_3	10.8	NaOH–$CsNO_3$	Yes	Not investigated
IV	1	Li, Cs ‖ OH, NO_3	22.0	LiOH–$CsNO_3$	Yes	Not investigated

which for that reason also deviates from the general regularity in change of thermal effect in the first group).

The alkali hydroxide-nitrate exchange decomposition is characterized by the occurrence of stratification in the six reciprocal systems (Figure 2). It is interesting that stratification is observed in the second, third and fourth groups, i.e., in those reciprocal systems formed by alkali metals between which one other metal is located in the periodic system (second group), between which are two other metals (third group), or between which are three other metals (fourth group). No stratification is observed in the first group of reciprocal systems. It is seen from Table 2 that we were unable to confirm all our conclusions experimentally (due to the absence of cesium compounds), but we are fully convinced of the validity of our conclusions regarding the systems Na, Cs‖ OH, NO_3 and Li, Cs ‖OH, NO_3, because they exhibit a more pronounced equilibrium shift than systems preceding them and the occurrence of stratification in them has been experimentally demonstrated. In our opinion, stratification must also occur in the system K, Cs‖ OH, NO_3, since it belongs to the second group, a characteristic of which is stratification. It is usually considered that stratification is observed in reciprocal systems with a large thermal effect (20 kcal and more). We consider that the magnitude of the thermal effect is by no means a criterion for anticipating stratification in reciprocal systems. Indeed in the alkali hydroxide-nitrate exchange decomposition, the system Li, Na ‖ OH, NO_3 has a thermal effect of 11.2 kcal and yet no stratification is observed in it, whereas the systems Na, Rb ‖ OH, NO_3 (thermal effect 7.9 kcal) and Na, Cs ‖ OH, NO_3 (thermal effect 10.8 kcal) are characterized by stratification.

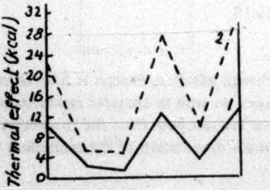

Figure 1. Halide exchange decomposition.
1) Lithium-sodium exchange decomposition;
2) lithium cesium exchange decomposition.

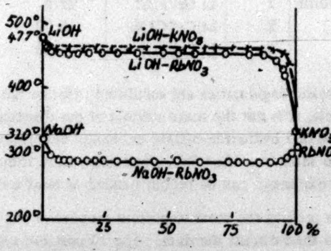

Figure 2; Alkali hydroxide-nitrate exchange decomposition with stratification.

If stratification is possible in a particular exchange decomposition (we are speaking of systems formed by metals of one group of the periodic system), then it will always be observed in those reciprocal systems which are formed by metals separated from each other in the periodic system by one, two or three elements. In the last case stratification will be at a maximum.

Experiments show that stratification is governed not only by the cations but also by the nature of the anions. Stratification is observed most frequently of all in reciprocal systems containing the NO_3' anion. For example, stratification is observed all along the stable diagonals of $TeNO_3$-AgCl, KNO_3-TlBr, KNO_3-TeI, as well as in the binary systems $NaNO_3$-AgCl, $NaNO_3$-AgBr, KNO_3-AgCl, KNO_3-AgBr. It is difficult to account for the special tendency of nitrates to form strata, but it is very probably associated with the low melting point of these compounds and the marked difference between their structure and that of the other component of the pair. We can expect this problem to be likewise clarified by further investigation of the reciprocal systems in other groups of the periodic system of the elements.

The following features are also very characteristic of alkali hydroxide-nitrate interchange: 1) occurrence of solid solutions on the sides formed by alkalis; 2) a fairly large number of compounds in the systems; 3) the largest crystallization field belongs as a rule to the component with the highest melting point; 4) congruent compounds exhibit a flat maximum; 5)some of the compounds are incongruent; 6) alkali hydroxides and nitrates formed by the same metals give compounds of the type of MOH, MNO_3, where M is an alkali metal. Compounds of this type may be regarded as acid salts of orthonitric acid H_3NO_4, in analogy with orthophosphoric acid H_3PO_4.

SUMMARY

1. Six reciprocal systems of the alkali hydroxide-nitrate exchange decomposition exhibit stratification.

2. Stratification is observed in systems formed by alkali metals which are separated from each other in the periodic system by one, two, or three elements.

3. Systems containing the NO_3' ion are particularly prone to stratification.

4. Stable pairs of the alkali hydroxide-nitrate exchange decomposition are systems formed from alkali hydroxides with low molecular weight and nitrates with high molecular weight.

The hydroxyl ion generally increases the number of compounds in the systems.

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PROPERTIES OF ACIDS AND BASES IN ACID SOLVENTS

V. POTENTIOMETRIC STUDY OF THE EFFECT OF ANHYDROUS FORMIC ACID ON THE STRENGTH OF ACIDS

A. M. Shkodin, N. A. Izmailov and N. P. Dzyuba

In the preceding papers it was shown that anhydrous formic acid has a high leveling effect on bases [1]. Both strong and extremely weak (in water) bases (pK about 13.8) acquire the same strength in formic acid. The number of substances developing basic properties in acid solvents in comparison with water has been considerably increased, this being bound up with the donor (protogenic) properties of acidic solvents.

Interest attaches to a study of the effect of acid solvents on the strength of acids. In this connection it is a general law that the number of substances possessing acidic properties in solvents with an acid character is considerably smaller than in water. The study of the individual properties of acidic solvents, however, has hitherto been neglected. Acidic solvents vary both in chemical and physical properties and these differences are bound to be reflected in the degree of their influence on the strength of acids.

In a series of papers it was established that acetic acid varies greatly in its effect. Organic acids which have high acidity in water (e.g. trichloracetic acid) become so weak in acetic acid that they do not titrate as acids [2] and exercise a negligible catalytic action [3]. This enabled us to effect fractional titration [2] of the mixture of acids:

$$HClO_4 - H_2SO_4,\ HClO_4 - HCl,\ CH_3C_6H_4SO_3H - HNO_3.$$

Formic acid differs markedly from acetic acid in the magnitude of its dielectric constant (57), which determines the electrostatic interaction of ions, as well as in the magnitude of the ionic product (pK_i of acetic acid is 12.6, that of formic acid is 6.3). It is therefore of interest to study the effect of formic acid on the strength of acids. In the first paper devoted to this problem, Zanninovich-Tessarin [4] arrived, on the basis of cryoscopic measurements, at the conclusion that the dissolved acids become associated in formic acid. The later investigations of Schlesinger [5] showed that anhydrous formic acid has a high dissociating action on salts and acids. An electroconductivity study of hydrochloric acid showed that the degree of dissociation of hydrogen chloride at a molar concentration of 0.0111 is 0.86, while at a concentration of 0.0518 M the value of α is 0.57.

Hammett and Deyrup [6] determined by an indicator method the strength (first constant) of sulfuric acid and benzene sulfonic acid. In this solvent they proved to be strong acids. The same authors obtained a value of $2 \cdot 10^{-5}$ for the second dissociation constant of sulfuric acid.

In the present investigation we attempted to obtain more systematic data for the effect of anhydrous formic acid on the strength of inorganic and organic acids, in view of the theoretical and practical importance of the problem.

EXPERIMENTAL

Anhydrous formic acid was prepared by the previously described method [1,5]. The following acids were studied:

$$HClO_4,\ HCl,\ H_2SO_4,\ CH_3C_6H_4SO_3H,\ CH_3COOH,\ CCl_3COOH,\ CH_2ClCOOH;$$

$$(NO_2)_3C_6H_2OH \text{ and } C_6H_4OHCOOH.$$

The first two of these were prepared by double-decomposition in formic acid:

$$Ba(ClO_4)_4 + H_2SO_4 \rightarrow 2HClO_4 + BaSO_4,$$

$$BaCl_2 + H_2SO_4 \rightarrow 2HCl + BaSO_4.$$

The starting salts were pure grades, twice recrystallized from water and absolute alcohol. Barium salts were selected because $BaSO_4$ is the least soluble of all barium salts in formic acid. The sulfuric acid was twice distilled over bichromate. Admixture of 1.7 % water to the prepared acid led to a content of 0.02% water in the prepared 0.1 M solutions. Special experiments showed that such an admixture of water does not affect the potential of the quinhydrone electrode, as was also noted by Hammett and Dietz [7]. The precipitates of barium sulfate were not removed as a precaution against absorption of moisture by the solvent during the later operations. As was shown in later experiments, the precipitate had no appreciable effect on the results of titration. The amounts of salts and sulfuric acid were so selected as to give 0.1 M solutions of $HClO_4$ and HCl. In this connection it transpired that the double decomposition between $Ba(ClO_4)_2$ and H_2SO_4 in formic acid does not proceed to completion; instead of the anticipated 0.1 M solution of chloric acid, a mixture of chloric and sulfuric acids is obtained with a total concentration of 0.0885 M, while the proportion of chloric acid is 87%. Solutions of the remaining acids were prepared by dissolving definite weights of the pure anhydrous substances. The technique of investigation consisted in potentiometric titration of 0.1 M solutions of the acids with 0.2 M pyridine solution (pure, freshly distilled material) with a lamp potentiometer. The vessel used for the titration ensured exclusion of atmospheric moisture and was identical with that used in earlier work [1]. The electrochemical cell compound.

$$\text{Pt}\ \underbrace{\left|\begin{array}{l}\text{acid}\\ \text{quinhydrone}\end{array}\right|\begin{array}{c}\text{KCl}\\ \text{satd.}\end{array}}_{\text{in HCOOH}}\ \Big|\ \underbrace{\begin{array}{c}\text{KCl}\\ \text{satd.}\end{array}\Big|\ \text{Hg}_2\text{Cl}_2\ \Big|}_{\text{in H}_2\text{O}}\ \text{Hg.}$$

Titration was performed with quinhydrone and glass electrodes. This was done not only because it was of interest to compare the obtained results and to secure supplementary evidence for the possibility of utilizing the glass electrode in nonaqueous (acidic) media, but also because hydrogen chloride in anhydrous formic acid reacts with quinhydrone and the mixture titrates like the pure solvent. The possibility of utilizing the quinhydrone electrode in formic acid solutions has already been demonstrated [1,7]. In our work the glass electrode has been repeatedly used for titration in acetic acid. Its potential was rapidly established and remained stable. The possibility of using it in acetic acid solution was demonstrated by the special investigations of Izmailov and Aleksandrova [8]. Attention should be drawn to one special feature of the glass electrode in acid solvents: The potential of the glass electrode during potentiometric titration remains stable for some time (10-15 titration curves), but subsequently the electrode potential is not stable. If the inner solution (Weibel solution) at the electrode is replaced by fresh solution, then the electrode functions again, and the potential is again stabilized but at a value considerably lower than the original potential in otherwise identical conditions.

The plots of titration of the acids at the quinhydrone and glass electrodes exhibit differences in the alkaline region (Fig.1). (We consider solutions containing an excess of $HCOO^-$ ions to be alkaline). The potential jump at the equivalent point is considerably lower for curves plotted with the glass electrode. However, the ratio of the dissociation constants of acids, calculated from the titration curves, was identical for both electrodes. We were thus able, on the basis of glass electrode data, to calculate the dissociation constant of HCl.

Consequently the glass electrode gives a serious error in formic acid in the alkaline region, and this limits its application in formic acid solutions.

Data have been published [5] for 0.1 M solutions of hydrogen chloride in anhydrous formic acid, but we failed to obtain reproducible results for these solutions; titration values varied the whole time even with a reduced amount of HCl, and only after keeping the solution for seven days were reproducible results obtained when titrating half the amount of introduced acid. Since pyridine and HCl form the compounds Py · 2HCl and Py · HCl, the half amount may be due to the formation of Py · 2HCl. This possibility was not confirmed, however, in titration with sodium formate, and we reached the conclusion that the variable results were due to volatilization of HCl. In the later experiments on HCl titration, therefore, we used 0.05 M solution. The potential of the glass electrode was then satisfactorily reproduced and the equivalence point on the curve was close to the theoretical value. The remaining acids did not introduce any complications.

In Fig. 2 are plotted the titration curves. Their character is that usual for acid-base titrations.

As in the previous cases the effect of formic acid on the strength of the acids was quantitatively evaluated by calculating the dissociation constants with the help of the Rciler equation [9].

$$\epsilon = 200\sqrt{K}\,\sinh\Delta,$$

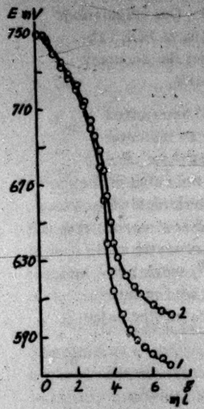

Fig. 1. Titration curves of toluenesulfonic acid in anhydrous formic acid. 1) With quinhydrone electrode; 2) with glass electrode.

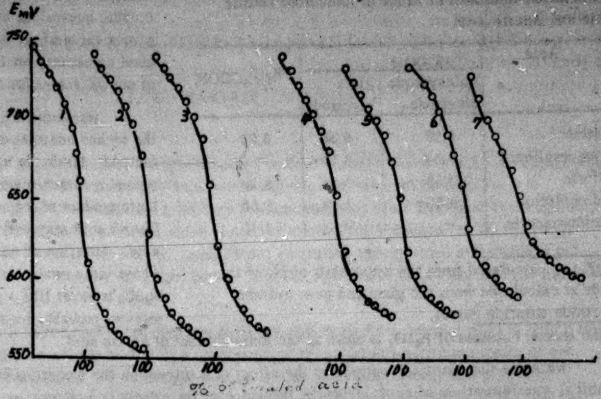

Fig. 2. Titration curves of acids in anhydrous formic acid. 1) Chloric; 2) toluenesulfonic; 3) sulfuric with quinhydrone electrode; 4) chloric; 5) toluenesulfonic; 6) sulfuric; 7) hydrochloric, with glass electrode.

where ϵ is the percentage titer error;
Δ is the potential jump in millivolts corresponding to the given titer error multiplied by 0.158;
K is K_i/C_AK_A, where K_i is the ionic product of the solvent; K_A is the sought for dissociation constant of the acid; C_A is the salt concentration at the stoichiometric point.

pK_i was calculated from the titration data in accordance with the procedure of Hammett and Dietz [7]. The value of pK_i was corrected for the salt error by the formula

$$pK_i = pK_i' + 2A\sqrt{\mu},$$

where pK_i' is calculated from the titration data;

$A = 0.5(D_{H_2O}/D_{HCOOH})^{3/2}$; D is the dielectric constant; μ is the ionic strength.

No correction is introduced for the error in the degree of dissociation, since the investigated acids and the base used for titration are substantially completely dissociated in formic acid. The resultant value of the ionic product of the solvent in presence of chloric acid (the strongest acid) was equal to 5.77 in the case of the quinhydrone electrode. This value was also taken for calculation of the dissociation constants of acids in the Roller formula cited above.

The obtained pK values for the acids are listed in the table side by side with the pK values of the same acids in acetic acid, calculated by Izmailov [10].

It was found that acetic acid, the chloroacetic acids, salicylic acid and picric acid are so weakened both in formic and acetic acid that they do not titrate as acids. This property may be exploited for fractional titration of mixtures of inorganic and organic acids in formic acid as solvent. Thus the utilization of this solvent both for determination of bases [1] and for fractional titration of acid mixtures widens the potential scope of acid-base titration.

The dissociation constant of HCl in formic acid was calculated from the conductometric data of

TABLE

Dissociation Constants of Acids in Anhydrous Formic Acid and Acetic Acid

Acid	pK_{HCOOH}		pK_{CH_3COOH}
	quinhydrone electrode	glass electrode	
Chloric	0.28	0.56	5.80
Toluenesulfonic	0.34	0.73	–
Sulfuric	0.58	0.94	8.20
Hydrochloric	0.89*	1.23	8.85
Trichloroacetic	–	–	11.46

* pK was calculated from the mean shift of pK of the acids as calculated from the glass and gum hydrone electrode titration curves.

Schlesinger and Martin [5]. The value of the constant for a concentration of 0.0518 M was 0.0385, equivalent to pK = 1.41. Our calculations give a value of pK = 1.23 for 0.05 M HCl. The good agreement for HCl indicates the accuracy of our pK values for the other acids.

Hammett and Deyrup [6] determined the second constant of H_2SO_4 by an indicator method. Since the value of $2 \cdot 10^{-5}$ for the second constant is very close to the value of the ionic product of the solvent, sulfuric acid in formic acid may only be titrated as a monobasic acid. Titration of sulfuric acid in acetic acid, whose ionic product is $2.5 \cdot 10^{-13}$, shows that H_2SO_4 behaves like a monobasic acid in this solvent, probably for the same reason (the value of the second constant of H_2SO_4 is close to the ionic product of acetic acid.

We know that Hantzsch correlated the effect of a solvent on the properties of acids mainly with the chemical transformations of acids under the influence of the solvent due to reaction of acid with solvent. Hantzsch relegated the physical properties of the solvent to a secondary place. Comparison, however, of the obtained data for acid strengths in acidic solvents (formic and acetic acids) is indicative of the very important role of the dielectric constant of the solvent. Inorganic acids in formic acid (DC = 57) are considerably weaker than in acetic acid (DC = 6). Whereas acetic acid alters the strength of inorganic acids to such a degree that some of them can be fractionally titrated, the inorganic acids which are strong in water remain strong in formic acid, although they become somewhat weaker than in water.

SUMMARY

1. A study was made by the method of potentiometric titration of the effect of anhydrous formic acid on the strength of inorganic and organic acids (chloric, sulfuric, hydrochloric, toluenesulfonic, trichloroacetic, monochloroacetic, picric, acetic and salicylic).

2. It was shown that inorganic acids remain strong in anhydrous formic acid; formic acid differs from acetic acid in not possessing a modifying effect on the strength of inorganic acids, due to the high dielectric constant of formic acid. Organic acids become so weak in formic acid that they do not titrate like acids. This characteristic may be utilized for fractional titration of mixtures of inorganic and organic acids.

3. The dissociation constants of chloric, sulfuric, hydrochloric and toluenesulfonic acids were calculated from the titration data.

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THE MOBILITY OF HYDROGEN IN SOME ORGANOSILICON COMPOUNDS

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Isotopic exchange of atoms in C–H bonds is strongly hindered or does not take place at all. An appreciable velocity is only observed when this bond is weakened by appropriate substituents, reagents or catalysts. In discussing the hindrance to exchange at C–H bonds, A. I. Brodsky [1] suggested that rapid hydrogen exchange only proceeds in presence of a free electron pair at an atom which is not the exchanging hydrogen (N, O, Cl, etc.). In such cases the exchange reaction is associated with an insignificant activation energy, since activation is not required for preliminary breaking of the element-hydrogen bond. Here the addition of deuterium and the removal of hydrogen occur simultaneously.

The carbon in compounds is surrounded by an electron shell not possessing free electron pairs to which the deuterium of a suitable donor might be able to add on at a greater speed than that at which the rupture of one of the C–H bonds takes place. Consequently this exchange calls for a high activation energy and proceeds relatively slowly and only when the C–H bond is weakened. These speculations are consistent with the marked inhibition of hydrogen exchange in H–H and B–H bonds, which are likewise not surrounded by free electron pairs, and in the ammonium ion [2] where, in contrast to ammonia or amines, all the electron pairs are bonded around an atom of nitrogen. In silicon compounds, as in compounds of its analog (carbon), all the electron pairs are similarly bonded. Thus the Si–H bond in organosilicon compounds should resemble the C–H bond in exchange susceptibility, and the study of isotopic exchange in these compounds may serve to confirm the correctness of the foregoing ideas. Such an investigation is also of interest in itself since it has not previously been undertaken.

In this investigation hydrogen exchange was studied in the Si–H bonds of the silanes $HSi(C_2H_5)_3$ and $HSi(C_6H_5)_3$ and of triethoxysilane $HSi(OC_2H_5)_3$. The hydrogen donors were heavy water, heavy ethyl alcohol C_2H_5OD, and heavy diethylamine $DN(C_2H_5)_2$.

The choice of the organosilicon compounds was dictated by their superior stability compared with unsubstituted silanes, by the presence of only one Si–H bond, and by the presence of substituents with differing degrees of electronegativity.

EXPERIMENTAL

The starting material, silicochloroform, $HSiCl_3$, was prepared by the action of dry hydrogen chloride on silicon at 300° [3]. After fractionation the product had b.p. 32°. Yield 44%.

Triethylsilane $HSi(C_2H_5)_3$ was prepared by reaction of silicochloroform with a Grignard reagent [4]. After fractionation the product had b.p. 107-108° and d_4^{20} 0.7301. Yield 52% of theory.

Under the action of alcoholic potassium hydroxide it is converted into triethylsilanol with b.p. 154-156° and d_4^{20} 0.8597; when boiled with 30% aqueous alkali it forms hexaethyldisiloxane with b.p. 223°; when the latter is heated with alcoholic alkali it is transformed into the same triethylsilanol.

Triphenylsilane $HSi(C_6H_5)_3$ was prepared by the same method [5]. After distillation under reduced pressure (b.p. 180° at 15 mm) the product solidified as a colorless crystalline mass with m.p. 36°. Yield 67%. Conflicting data about triphenylsilane have appeared in the literature. Ladenburg [6] claimed to have prepared triphenylsilane in the form of crystals with m.p. 200-203° from the corresponding bromide by the action of an alkyl zinc in a sealed tube. Kipping and Murray [7] prepared triphenylsilane by destructive distillation of cyclosilicotetrane $Si_4(C_6H_5)_8$ in the form of an oil which did not solidify at 0° and which was converted by HBr into $(C_6H_5)_3SiBr$; the latter with 5% NaOH gave triphenylsilanol. Reynolds, Bigelow, and Kraus [5], whose method we repeated for the synthesis, considered the results of the earlier authors to be erroneous and that Kipping had only obtained a very impure triphenylsilane as evidenced by the oily form.

Andrianov and Sobolevsky recently [8] drew attention to the need for checking the data on this compound. Our results have confirmed that Reynolds and co-workers actually prepared pure triphenylsilane.

For the purpose of identification of our preparation, it was converted by boiling with alcoholic alkali into a substance which after three recrystallizations from ligroin melted at 151°. It did not depress the melting point of triphenylsilanol prepared from $SiCl_4$ and $MgBrC_6H_5$ [9]. Digestion of our preparation with 30% aqueous alkali gave hexaphenyldisiloxane with m.p. 222°, which with alcoholic alkali is converted into the same triphenylsilanol.

Triethoxysilane $HSi(OC_2H_5)_3$ was prepared in benzene solution from $HSiCl_3$ and absolute alcohol [10]. The fractionated product had b.p. 134° and d_4^{20} 0.8753; yield 43% of theory.

In the work in question [10] it was found that an increase in the period of standing of the reaction mixture led to an increase in the amount of by-product $Si(OC_2H_5)_4$ at the expense of the main product. This has been ascribed to the reactions:

$$HSi(OC_2H_5)_3 + HCl \longrightarrow ClSi(OC_2H_5)_3 + H_2;$$

$$ClSi(OC_2H_5)_3 + C_2H_5OH \longrightarrow Si(OC_2H_5)_4 + HCl.$$

According to the same authors, however, the yields did not fall when HCl was passed through in a nitrogen stream. We found that pure $HSi(OC_2H_5)_3$ is converted to a very large extent into $Si(OC_2H_5)_4$ when heated in sealed glass ampoules with alcohol. Lowering of the temperature increases the amount of unreacted material. The reaction proceeds to a slight extent even in the cold. When the ampoules are opened a brown gas escapes which had been dissolved under pressure in the liquid. For conclusive demonstration of the interaction of $HSi(OC_2H_5)_3$ with alcohol, we heated two ampoules at 100° for 125 hours. The first ampoule contained pure $HSi(OC_2H_5)_3$, which remained unchanged after heating; the second contained $HSi(OC_2H_5)_3$ and absolute alcohol. When the latter was heated about one-half of the triethoxysilane was converted into $Si(OC_2H_5)_4$ with b.p. 165-166° and d_4^{20} 0.9308. Hence $HSi(OC_2H_5)_3$ reacts with alcohol according to the nucleophilic scheme:

$$HSi(OC_2H_5)_3 + C_2H_5OH \longrightarrow H_2 + Si(OC_2H_5)_4.$$

Isotopic exchange was conducted in sealed glass ampoules placed in a thermostat. Conditions were selected in which the silanes were relatively stable. Water forms a two-phase system with triethylsilane and triphenylsilane. With alcohol the first forms a homogeneous solution; with diethylamine both give homogeneous solutions. In some experiments the exchange with water was performed in homogeneous pyridine and dioxan solution. Triethoxysilane forms a homogeneous solution with alcohol. After completion of exchange the components were separated. Since the silanes contain a large number of unexchanged hydrogen atoms per atom of exchanged hydrogen, the relative change of density of alcohol or water, even with complete exchange would be small. After the exchange, therefore, the deuterium content of the silane was determined. The material was calcined and the deuterium content of the resultant water was determined by the flotation method. The deuterium content of the alcohol and diethylamine was similarly determined. The experimental results are presented in Tables 1 and 2.

TABLE 1

Isotopic Exchange of Hydrogen in Triethylsilane

Donor	Catalyst	Temp.	Duration (hrs)	Water density (in γ units)		
				initial*	from combustion	
					complete exchange of one hydrogen; calculated	found
D_2O	–	116°	51	2670	165	0
D_2O	H_2SO_4	116	49	2670	163	0
D_2O	KOH	116	70	2670	164	4
D_2O + pyridine	–	116	50	22000	1220	7
D_2O + dioxan	–	100	12	3500	212	15
D_2O + dioxan	H_2SO_4	100	15	3500	211	6
C_2H_5OD	–	100	25	7000	296	0
C_2H_5OD	CH_3COONa	116	117	7000	346	0
C_2H_5OD	$KHSO_4$	118	146	7000	340	0
$DN(C_2H_5)_2$	–	78	18	16130	656	0

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* In the case of alcohol the D content of the hydroxyl group; in the case of diethylamine the D content of the NH group.

TABLE 2

Isotopic Exchange of Hydrogen in Triphenylsilane and Triethoxysilane

Donor	Catalyst	Temp.	Duration (hours)	Water density (in γ units)		
				initial*	from combustion	
					complete exchange of one hydrogen; calcd.	found
			Triphenylsilane			
D_2O	–	18	335	6550	306	5
D_2O	–	90	15	6550	250	7
D_2O	–	103	20	6500	306	12
D_2O	–	118	71	2670	164	7
D_2O	H_2SO_4	103	20	6550	332	6
D_2O	H_2SO_4	118	69	2670	165	0
D_2O	NaOH	103	18	6500	340	13
D_2O + dioxan .	–	100	11	3500	211	4
D_2O + dioxan .	H_2SO_4	100	15	3500	212	0
$DN(C_2H_5)_2$ ...	–	20	50	16130	738	8
$DN(C_2H_5)_2$ ...	–	78	10	16130	728	10
			Triethoxysilane			
C_2H_5OD	–	20	49	7000	350	2

The triethylsilane was separated from water in a separating funnel, dried over $CaCl_2$ and fractionated. Difficulties accompanied its separation from alcohol because an azeotropic mixture boiling at about 65° is formed. Consequently as soon as the absence of exchange with water had been established, the alcohol was washed out with water. The pyridine and dioxan were likewise washed out. After exchange with diethylamine, the triethylsilane was fractionated, washed with water, and dried over $CaCl_2$.

The water or alcohol was distilled off from triphenylsilane and triethoxysilane with benzene, as suggested by Dean and Stark, or in vacuum. Diethylamine was separated by distillation. In all cases the $HSi(C_6H_5)_3$ was purified by vacuum distillation.

$HSi(C_2H_5)_3$ at room temperature in homogeneous alcoholic or aqueous dioxan solutions decomposes with loss of hydrogen when a small quantity of alkali is added. The OC_2H_5 ion has the same effect. This is not observed in pyridine. The catalyst selected for experiments on alkaline catalysis during exchange with heavy alcohol was therefore the weak base CH_3COONa.

$HSi(C_6H_5)_3$ which has been homogenized reacts even more vigorously with alkali, losing hydrogen even in aqueous pyridine solution. $HSi(OC_2H_5)_3$ reacts in a beaker even with a base such as alcohol (see above).

The data presented, and certain other data, have limited the possibility of conducting exchange experiments in the conditions specified in the tables.

EVALUATION OF RESULTS

From the above results we can conclude that even after prolonged heating with acid or alkali not one of the three investigated silanes undergoes exchange with heavy water, heavy alcohol or heavy diethylamine. The negligible content of deuterium found in the silanes in some experiments does not exceed a few percent of the amount anticipated for complete exchange and may be ascribed to retention of traces of water.

The analogous carbon compounds exhibit the same behavior in respect to exchange. Triphenylmethane does not exchange hydrogen with heavy water after 144 hours at 100° in presence of alkali [11]; isobutane only gives a slow exchange with 100% sulfuric acid containing tritium [12]. The exchange of an orthoformic ester has not been investigated.

In conformity with its position in the periodic system, silicon is less electronegative than carbon. The electronegativity of carbon is greater than that of hydrogen, and this brings about partial polarization of the $\bar{C}-\overset{+}{H}$ bond susceptible to electrophilic reactions. When electrons are removed by electronegative substituents, ionization of the hydrogen may occur. Conversely, the electronegativity of silicon is less than that of hydrogen, and hence the bond is polarized in the reverse direction: $\overset{+}{\bar{Si}}-H$. In this case exchange by an electrophilic mechanism is not very probable, and this also makes nucleophilic substitution improbable. Thus, compounds of the type of R_3SiH react nucleophilically toward caustic alkali, amides of metals, alcoholates, etc. The concept of nucleophilic substitution reactions in silicon compounds is consistent with the possibility of complex formation with probable completion of the outer electron shell of Si to a value of 12 (SiF_6^{--}, salts of siliconium).

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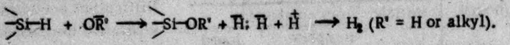
* In the case of alcohol the D content of the hydroxyl group; in the case of diethylamine the D content of the NH group.

In compounds of the R_3SiH type electronegative substituents (R= C_6H_5, OC_2H_5), which do not cause ionization, increase the positive charge on the Si atom, thereby accelerating the reaction of nucleophilic substitution of the type of

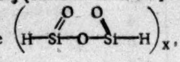


$$\rangle Si-H + O\bar{R'} \longrightarrow \rangle Si-OR' + \bar{H}; \bar{H} + \overset{+}{H} \longrightarrow H_2 \text{ (R' = H or alkyl).}$$

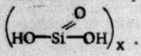
In the case of $HSi(C_6H_5)_3$ the OH ion concentration of aqueous pyridine solution is adequate for this reaction, while $HSi(OC_2H_5)_3$ reacts even with a weak base such as alcohol. In the light of this reaction we can understand the notable increase of yield in the synthesis of trialkoxysilanes in passing from ethyl to butyl [10]. Actually the increasing chain length of the alkyl radical increases its positive inductive effect, thereby reducing the positive charge on the silicon atom of the $\overset{+}{Si}-\bar{H}$ bond, and in turn the susceptibility to the nucleophilic substitution reaction. Fluorine is even more negative than ethoxyl, and consequently the positive charge on the silicon in $HSiF_3$ is greater than in $HSi(OC_2H_5)_3$ and $HSiCl_3$. The consequence of this is that when $HSiF_3$ reacts with alcohol [13] we obtain only $Si(OC_2H_5)_4$ and no $HSi(OC_2H_5)_3$:

$$2HSiF_3 + 4C_2H_5OH \longrightarrow Si(OC_2H_5)_4 + H_2SiF_6 + H_2.$$

Similarly $HSiCl_3$ (chlorine is more positive than fluorine) reacts with water in the cold to give polymeric silicoformic anhydride



$\left(H-\overset{O}{\overset{\|}{Si}}-O-\overset{O}{\overset{\|}{Si}}-H\right)_x$, which contains the SiH group, while $HSiF_3$ gives silicic acid



$\left(HO-\overset{O}{\overset{\|}{Si}}-OH\right)_x$.

The possibility of a radical mechanism cannot be excluded for hydrogen exchange in the Si–H bond if we remember that its energy is 12 kcal lower than that of the C–H bond. Up to now no convincing evidence has been obtained of a nucleophilic mechanism of hydrogen exchange of isotopes, for which a source of H^- ions is necessary. The probability of such a mechanism is limited by the low stability of the negative hydrogen ion or of the intermediate hydride complexes.

I thank Acting Member of the Academy of Sciences of the Ukrainian SSR, A. I. Brodsky for guidance and assistance in this research.

SUMMARY

1. Hydrogen exchange is shown not to take place in the compounds $HSi(C_2H_5)_3$, $HSi(C_6H_5)_3$ and $HSi(OC_2H_5)_3$ with D_2O, C_2H_5OD and $DN(C_2H_5)_2$, even under prolonged heating in presence of acids and bases.

2. These data bring the Si–H bond within the terms of A. I. Brodsky's earlier theory of isotopic hydrogen exchange.

3. Reaction was found to occur between triethoxysilane and alcohol with hydrogen exchange at the ethoxy group.

4. Considerations are put forward which explain the absence of exchange in the above-mentioned compounds and some peculiarities of substitution reactions at Si–H bonds.

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REACTIONS OF HYDROXIDES OF ARYL MERCURY

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3

In our previous paper [1] on the photochemical reactions of phenylmercury hydroxide in various solvents, a theory was put forward for the dissociation of the hydroxide into the hydroxyl radical and the phenylmercury radical. The latter radical reacted with the halogen contained in the solvent to form phenylmercury halide; in halogen-free solvents (alcohol, ethyl cellosolve) metallic mercury separated out and benzene was formed; in benzene solution diphenyl was formed. Separation of mercury may be considered to proceed by one of two routes: 1) Directly from the phenylmercury radical; or 2) through intermediate formation of diphenylmercury which reacts further by the usual scheme [2]. Cleavage of Hg from the C_6H_5Hg radical is extremely probable. We know that methylmercury prepared by electrolysis rapidly breaks down at the ordinary temperature into mercury and dimethylmercury [3].

In order to resolve this problem, experiments were conducted with phenylmercury hydroxide in solution in ethyl cellosolve and benzene. The reaction did not proceed to the end; irradiation was stopped when mercury began to separate. Diphenylmercury was found in solution in quantity equivalent to the separated mercury (Table 2, experiments 1 and 2).

$$C_6H_5HgOH + h\nu \longrightarrow C_6H_5Hg^{\cdot} + OH^{\cdot}$$

$$2C_6H_5Hg^{\cdot} \longrightarrow (C_6H_5HgHgC_6H_5) \longrightarrow (C_6H_5)_2Hg + Hg.$$

$$(C_6H_5)_2Hg + h\nu \longrightarrow C_6H_5Hg^{\cdot} + C_6H_5^{\cdot} \text{ etc.}$$

It may here be permissible to suggest a symmetrization reaction of the phenylmercury hydroxide by analogy with the symmetrizations of unsymmetrical mercury derivatives. With a view to checking this hypothesis experiments were performed on the thermal decomposition of the hydroxide in methanol solution. Among the reaction products apart from metallic mercury, benzene and formaldehyde, was found diphenylmercury in amount of 12-25% (Table 1). These data conclusively point to symmetrization of phenylmercury hydroxide during thermal reactions.

However, if the symmetrization of the hydroxide were to be effected in presence of ultraviolet light, then in halogen-containing solvents the yield of phenylmercury halide should not exceed 50%. Actually up to 80% of phenylmercury iodide was obtained in the photochemical reaction of phenylmercury hydroxide in a mixture of benzene and iodobenzene. We can therefore assume that diphenylmercury is formed photochemically by the above scheme.

In this investigation a study has also been made of the photochemical reactions of arylmercury hydroxides containing various substituents in the benzene ring. As with phenylmercury hydroxide the reactions in ethyl cellosolve proceed according to the general equation:

$$RC_6H_4HgOH + HOCH_2CH_2OC_2H_5 + h\nu \longrightarrow C_6H_5R + Hg + H_2O + 2CH_3CHO,$$

where R = o- and p-CH_3; n-$(CH_3)_2N$.

Mesitylmercury hydroxide reacts in the same way (Table 2, experiments 3-6).

In benzene solution the hydroxides of o- and p-tolylmercury give the same products as phenylmercury hydroxide in toluene: methyldiphenyl, water and mercury, i.e. substitution takes place in the benzene ring (Table 2, experiments 7 and 8).

Mesitylmercury hydroxide did not react with benzene even after very prolonged irradiation (200 hours). The difference between mesitylmercury hydroxide and the other hydroxides investigated was also reflected in its photochemical reactions with chloroform and carbon tetrachloride. The mesitylmercury chloride anticipated by analogy was not detected. Mesitylene was found in the chloroform solution and chloromesitylene in the carbon tetrachloride solution. An organomercury compound insoluble in common solvents was obtained in the latter experiment and must have been formed by cleavage of the hydroxyl from the $(CH_3)_3C_6H_2Hg\cdot$ Radical.

In both solvents mercuric chloride and calomel were formed due to the chlorinating action of the solvent on mercury under irradiation. These characteristics of the mesityl radical were previously manifested in the photochemical reactions of dimesityl mercury [4] (Table 2, experiments 9 and 10).

TABLE 1

Substance used		Period of heating (hours)	Temp. of heating (°C)	Obtained					
C_6H_5HgOH (g)	CH_3OH (ml)			mercury		diphenyl mercury		benzene (g)	formaldehyde (g)
				g	%	g	%		
2.5	20	70	180-185	1.25	73.6	0.75	24.9	0.08	0.2
3.0	20	24	200	1.78	88.2	0.45	12.4	0.36	0.3

Note. In these experiments benzene was identified by conversion to m-dinitrobenzene; formaldehyde was identified in the form of the dimedon derivative with m.p. 188°.

TABLE 2

Expt. No.	Materials taken				Irradiation period (hours)	Obtained	
	Hydroxides		Solvents			unchanged hydroxide	
	Formula	Quantity (g)	Name	Quantity (ml)		g	%
1	C_6H_5HgOH	3	Ethyl cellosolve	10	3	2.5	83.3
2	C_6H_5HgOH	2	Benzene	20	25	1.4	70.0
3	$o\text{-}CH_3C_6H_4HgOH$.	1.2	Ethyl cellosolve	15	18	–	–
4	$p\ CH_3C_6H_4HgOH$.	2	Ethyl cellosolve	15	22	–	–
5	$(CH_3)_3C_6H_2HgOH$.	1.5	Ethyl cellosolve	15	10	–	–
6	$(CH_3)_2NC_6H_4HgOH$	2	Ethyl cellosolve	4	12	–	–
7	$o\text{-}CH_3C_6H_4HgOH$.	1.8	Benzene	15	60	0.45	25.0
8	$p\ CH_3C_6H_4HgOH$.	1.8	Benzene	25	100	0.55	30.6
9	$(CH_3)_3C_6H_2HgOH$.	1.5	Chloroform	12	70	–	–
10	$(CH_3)_3C_6H_2HgOH$.	1.3	Carbon tetrachloride	15	60	–	–

TABLE 3

Expt. No.	taken					Duration of irradiation (in hours)
	C_6H_5HgOH	Solvent				
		1st component		2nd component		
		name	(ml)	name	(ml)	
1	3	Benzene	10	Iodobenzene	10	80
2	2	Benzene	20	Ethyl cellosolve	5	15
3	1.8	Benzene	25	Isopropyl alcohol	5	80
4	2.5	Benzene	20	Carbon tetrachloride	12	130

We were unable to clarify the reaction of p-dimethylaminophenylmercury with carbon tetrachloride. Mercury, mercuric chloride and calomel were found after irradiation of the solution; a dye was also obtained, probably a member of the triphenylmethane series, which gave violet solutions in acetone and benzene. The color changed to green under the action of acids.

We see from the experimental data that the behavior of the radicals formed on photolysis depends on the nature of the substituent, i.e., whether reactions involving removal of hydrogen or halogen take place, while in aromatic solvents substitution reactions take place. It therefore appeared of interest to perform photochemical reactions of phenylmercury hydroxide in a mixture of two solvents in order to establish the direction of the reaction in a given case. Phenylmercury iodide, diphenyl and water were formed in the photochemical reaction of phenylmercury hydroxide with iodobenzene and benzene. On the basis of the obtained data we may suggest that benzene entered into reaction with hydroxyl to form the phenyl radical:

$$C_6H_5HgOH + C_6H_5I + h\nu \longrightarrow C_6H_5HgI + C_6H_5C_6H_5 + H_2O.$$

Mercury separated when the reaction was carried out in a mixture of benzene and ethyl cellosolve; acetaldehyde was detected and a small amount of diphenyl.

The irradiation of a solution of phenylmercury hydroxide in a mixture of benzene and carbon tetrachloride led to separation of phenylmercury chloride, calomel, mercuric chloride, hexachloroethane, water and benzotrichloride, (the latter was identified by conversion to benzoic acid). Formation of benzotrichloride proceeds either at the expense of entry of the CCl_3 radical into the benzene ring, as happened in the studies of Nesmeyanov, Pecherskaya and Uretskaya [5], or as the result of addition of two radicals – $CCl_3^{\cdot}$ and phenyl (Table 3).

We thus see that photochemical reactions in a mixture of solvents proceed according to complex schemes. The course of the reaction may be accurately followed with the help of labeled atoms.

EXPERIMENTAL

1. Thermal reaction of phenylmercury hydroxide in methyl alcohol. The reaction mixtures were heated in sealed ampoules. The reaction products were identified by determination of their boiling points and of the melting points in admixture with pure substances. The experimental results are set out in Table 1.

TABLE 2

Obtained									
Product			Hg		$HgCl_2$		Hg_2Cl_2		Other products
Formula	g	%	g	%	g	%	g	%	
$(C_6H_5)_2Hg$	0.13	–	0.10	–	–	–	–	–	
$(C_6H_5)_2Hg$	0.07	–	0.09	–	–	–	–	–	0.05 g diphenyl
$C_6H_5CH_3$	0.30	82.6	0.67	87.0	–	–	–	–	Acetaldehyde
$C_6H_5CH_3$	0.45	76.1	1.25	96.1	–	–	–	–	Acetaldehyde
$C_6H_3(CH_3)_3$	0.40	75.4	0.82	92.1	–	–	–	–	Acetaldehyde
$C_6H_5N(CH_3)_2$*	0.60	65.0	1.10	92.4	–	–	–	–	Acetaldehyde
o-$CH_3C_6H_4C_6H_5$	0.60	65.0	0.75	91.4	–	–	–	–	Water
p-$CH_3C_6H_4C_6H_5$	0.30	84.7	0.65	80.2	–	–	–	–	Water
$C_6H_3(CH_3)_3$	0.41	77.3	–	–	0.28	23.4	0.78	74.1	C_2Cl_6
$C_6H_2Cl(CH_3)_3$	0.17	32.8	–	–	0.15	14.2	0.30	34.8	C_2Cl_6, organomercury compound

TABLE 3

Obtained										
C_6H_5HgX		Product		Hg		$HgCl_2$		Hg_2Cl_2		Other products
g	%	Formula	g	g	%	g	%	g	%	
3.2	80.1	$(C_6H_5)_2$	0.30	–	–	–	–	–	–	Water
–	–	$(C_6H_5)_2$	0.08	1.3	95.1	–	–	–	–	Acetaldehyde
–	–	$(C_6H_5)_2$	0.01	0.22	18.0	–	–	–	–	Acetone
0.50	18.8	$C_6H_5CCl_3$	0.09	–	–	0.88	44.1	0.70	34.9	Hexachloroethane

2. Photochemical reactions of arylmercury hydroxides in solutions. Experiments were performed in quartz test tubes which were irradiated at room temperature with a PRK-2 quartz mercury lamp. The experimental results are set out in Table 2.

Notes. 1. The percent yield of mercury and methyldiphenyl in experiments 7 and 8 were calculated on the basis only of the hydroxide entering into reaction.

2. The o- and p-methyldiphenyls in these reactions were identified by oxidation to the corresponding diphenyl carboxylic acids whose constants were then determined.

3. The products obtained in experiments 3-6 were identified by boiling point determinations

(Sivolobov's method). Subsequently the toluene (in experiments 3 and 4) was oxidized to benzoic acid with m.p. 121°; mesitylene was nitrated to 2,4,6-trinitro-1,3,5-trimethylbenzene with m.p. 233°; dimethylaniline was identified as its picrate, m.p. 162°.

4. Mesitylene and chloromesitylene (in experiments 9 and 10) were also identified by nitration to 2,4,6-trinitro-1,3,5-trimethylbenzene with m.p. 178°.

5. Mercuric chloride (Table 2, experiments 9 and 10; Table 3, experiment 4) was washed out with hot water and precipitated in the form of mercury sulfate. Calomel was identified by its qualitative reactions.

6. The melting points of hexachloroethane were determined in sealed capillaries (m.p. 183°).

3. Photoreactions of phenylmercury hydroxide in mixed solvents. The experimental results are presented in Table 3.

Notes. 1. The reaction products (columns 8 and 9) were identified by mixed melting point determinations.

2. The molecular weight of the obtained diphenyl (expt. 1) was found to be 155.4 (calculated 154).

3. Benzotrichloride (expt. 4) was isolated by conversion into benzoic acid (m.p. 121°), which was then titrated with alkali.

SUMMARY

1. Breakdown of the $C_6H_5Hg^{\cdot}$ radical when phenylmercury hydroxide is irradiated with ultraviolet light proceeds through formation of diphenylmercury.

2. The photoreactions of the hydroxides of o- and p-tolylmercury, mesitylmercury, and p-dimethylaminophenylmercury in ethyl cellosolve were investigated. These reactions proceeded in a similar manner to the reactions of phenylmercury hydroxide.

3. The reactions of o- and p-tolylmercury hydroxides in benzene were investigated. These photoreactions proceed with formation of methyldiphenyl due to a substitution reaction.

4. The photoreactions of mesitylmercury hydroxide were investigated. Irradiation of this compound in chloroform solution leads to formation of calomel, mercuric chloride, mesitylene and hexachloroethane. In carbon tetrachloride the products are calomel, chloromesitylene, hexachloroethane and an organomercury compound.

5. The following results were obtained in the photoreaction of phenylmercury hydroxide:

a) In benzene-iodobenzene mixture, phenylmercury iodide, diphenyl and water were obtained.

b) In benzene-ethyl cellosolve mixture, mercury, diphenyl and acetaldehyde were obtained.

c) In a mixture of benzene and carbon tetrachloride, the products were phenylmercury chloride, calomel, mercuric chloride, hexachloroethane and benzotrichloride.

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THE PROBLEM OF THE STRUCTURE OF GUSTAVSON'S HYDROCARBON

III. THE ACTION OF ZINC DUST ON TETRAHALONEOPENTANES

Ya. M. Slobodin and I. N. Shokhor

As far back as 1896, G. G. Gustavson [1-3] showed that zinc dust acts on tetrabromoneopentane to form a hydrocarbon with the composition C_5H_8. Later investigations of Demyanov, Favorsky, Filippov Whitmore and others established that Gustavson's hydrocarbon is a mixture consisting of methylenecyclobutane and 2-methyl-1-butene. Additional factors may lead to the formation, apart from the above-mentioned compounds, of spiropentane and very small amounts of 1,1-dimethylcyclopropane. Thus when tetrabromoneopentane is treated with zinc dust in aqueous ethanol, a mixture is formed which consists solely of methylenecyclobutane and 2-methyl-1-butene [4]. In aqueous methanol there is formed, in addition, a small quantity of spiropentane [5]. Addition of zinc bromide shifts the reaction in the direction of preferential formation of methylenecylcobutane [6].

Hass and McBee [7] investigated the conditions of formation of cyclopropane from 1,3-dichloropropane and found that optimum yields (95%) are obtained by cleavage of halogen in aqueous ethanol in presence of sodium carbonate and sodium iodide. The same results are obtained on substituting anhydrous acetamide for aqueous ethanol. It was also found that the substitution of one or both atoms of chlorine in 1,3-dichloropropane by iodine leads to better yields of the hydrocarbon. It is evident that the role of sodium iodide is to introduce iodine ions which undergo double decomposition with the molecule of 1,3-dichloropropane. The sodium carbonate serves to regenerate the iodine ions formed by reaction of the weakly dissociated zinc iodide.

The application of these conditions to tetrabromoneopentane led to the formation of spiropentane [5]. Dehalogenation in fused acetamide (170-180°) in presence of sodium carbonate and sodium iodide gave a hydrocarbon in 38% yield and with a spiropentane content of 47-60%. Using the same additives in aqueous ethanol, the yields of hydrocarbon were 78-79%. It contained 28% spiropentane, 56% methylene-cyclobutane, 18% 2-methyl-1-butene and about 1-3% of 1,1-dimethylcyclopropane [8]. Consequently, the conditions favoring closure of the cyclopropane ring also promote the formation of spiropentane.

In the present investigation a study was made of the effect of the nature of the halogen atom (Cl, Br, I) on the composition of the hydrocarbon mixture formed by the action of zinc dust on tetrahaloneopentanes in dilute alcohol and in dilute acetamide with and without additions of sodium carbonate and sodium iodide. In order to avoid secondary reactions the volatile products were immediately distilled off from the reaction mixture.

The composition of the hydrocarbon mixture was determined in each experiment with the help of Raman spectra. Visual comparison of the intensities of the spectral lines enabled the composition of the mixture to be determined to an accuracy of only up to 10%, but even this relatively rough analysis permitted certain regular characteristics in the series of tetrahalo derivatives of neopentane to be established.

No dehalogenation occurred when zinc dust acted on tetrachloroneopentane in presence of sodium carbonate in dilute alcohol, and the whole of the starting material was recovered unchanged. When the alcohol was replaced by ethylene glycol the reaction proceeded very sluggishly even at 180-190°. A minute amount of a hydrocarbon and an unsaturated chloride with b.p. about 80° were formed. Nearly half of the original material was recovered unchanged. A definite reaction took place only when using anhydrous acetamide. In presence of sodium carbonate at 170-180° a hydrocarbon mixture was obtained which boiled at 33-42°. The Raman spectrum contained lines whose frequencies coincided with those attributed in the literature to mixtures of spiropentane, methylenecyclobutane and 2-methyl-1-butene [5,11,12]. The composition of the hydrocarbon mixture was methylenecyclobutane 80-85%, spiropentane 10%, 2-methyl-1-butene 5-10%.

In presence of sodium carbonate and sodium iodide, the content of spiropentane, as was to be expected, rose to 30-40%, that of 2-methyl-1-butene rose to 10-20%, and the methylenecyclobutane content fell to 50% (Table 1).

TABLE 1

Dehalogenation of Tetrachloroneopentane

Method of preparation of the hydrocarbon	Total yield of hydrocarbons (%)	% Content		
		spiropentane	methylene-cyclobutane	2-methyl-1-butene
In acetamide in presence of sodium carbonate. .	40	10	80-85	5-10
In acetamide in presence of sodium carbonate and sodium iodide	40-50	30-40	50	10-20

TABLE 2

Dehalogenation of Tetrabromoneopentane

Method of preparation of hydrocarbon	Total yield of hydrocarbons (%)	% Content			
		spiropentane	methylene-cyclobutane	2-methyl-1-butene	1,1-dimethyl-cyclopropane
In aqueous ethanol (Gustavson's method [13]	80	–	80-90	10-15	–
In aqueous ethanol in presence of sodium carbonate and sodium iodide [8]	78-89	24-28	54-58	13-18	1-3
In acetamide in presence of sodium carbonate	40	20-30	50-60	10-20	–
In acetamide in presence of sodium carbonate and sodium iodide [8]	38	47-60	36-10	17-30	–

Results of dehalogenation of tetrabromoneopentane are set out in Table 2.

Tetraiodoneopentane in aqueous alcohol reacts with zinc dust very slowly. In fused acetamide in presence of sodium carbonate and sodium iodide a mixture of hydrocarbons containing 50% spiropentane is formed. The amount of spiropentane does not change even when the reaction is performed in acetamide without sodium carbonate and sodium iodide (Table. 3).

TABLE 3

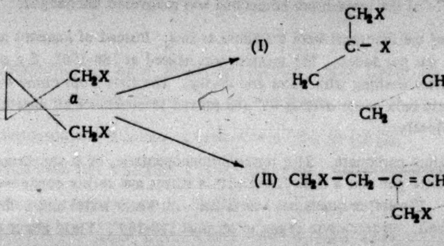
Dehalogenation of Tetraiodoneopentane

Method of preparation of the hydrocarbon	Total yield of hydrocarbons(%)	% Content		
		spiropentane	methylene-cyclobutane	2-methyl-1-butene
In acetamide in presence of sodium carbonate and sodium iodide.	80	50	40	10
In acetamide without additives	80	50	25	25

A comparison of the tabulated data permits the conclusion to be drawn that in anhydrous acetamide in presence of sodium carbonate the yields of spiropentane increase as we pass from tetrachloro- to tetraiodoneopentane, the tetrabromo-compound occupying an intermediate position. Additions of sodium carbonate considerably increase the yields of spiropentane from tetrachloro- and tetrabromoneopentanes. Addition of sodium carbonate has no influence on the yield of spiropentane from tetraiodoneopentane, which fact confirms its role as a medium promoting the regeneration of iodine ions in the reaction. Yields of 2-methyl-1-butene increase as we pass from the tetrachloro- to the tetraiodo- compound. It may be suggested that the increase in yields of spiropentane is related to the magnitude of the atomic radii of the halogens.

1,1-Dihalodimethylcyclopropane must be an intermediate product of the dehalogenation of the tetrahaloneopentanes. The formed trimethylene ring with a valency angle of 60° causes expansion of the outer valency angle [14,15]. Thus, we know from electronographic data that the H-C-H angle in cyclopropane is 118° [14]. The enlargement of the valency angle α in 1,1-dihalodimethylcyclopropane greatly hinders the closure of the second three-membered ring and in turn hinders the formation of spiropentane.

In addition, the formed 1,1-dihalodimethylcyclopropane, possessing a well-known isomerization tendency, may undergo isomerization in two directions:

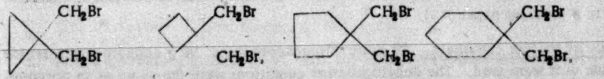


The dihalo derivative of the cyclobutane series formed by the first alternative readily reacts with zinc dust to form methylenecyclobutane, whereas the unsaturated dihalo derivative formed by the second route and containing halogen atoms in positions 1 and 4 will be largely subjected, as follows from Demyanov's researches [16], to reduction to 2-methyl-1-butene and only in small degree to cyclization.

Introduction of iodine ions into the reaction mixture leads to substitution of iodine for one or both of the halogen atoms both in dichlorodimethylcyclopropane and in dibromodimethylcyclopropane. Since the bromine possesses the greater atomic radius, it will facilitate closure of the second cyclopropane ring and thereby lead to increased yields of spiropentane.

At the same time the enhanced tendency of α-iodo derivatives to rupture of the three-membered ring [17] leads to some increase in yields of the open-chain hydrocarbon, 2-methyl-1-butene.

It follows from the above considerations that in the dibromodimethylcyclane series



closure of the three-membered ring will occur most readily in dibromodimethylcyclohexane, and with the most difficulty in dibromodimethylcyclopropane. And indeed the formation of spiro-(2,5)-octane takes place in a yield of 91% [18].

In previous communications [19,20] we showed that α-halo derivatives of the cyclopropane series readily isomerize to unsaturated open-chain halo derivatives. This change is quantitative for iodo derivatives, less pronounced for bromo derivatives, and least pronounced for chloro derivatives. It follows from the data of the present investigation that in the case of 1,1-dihalodialkylcyclopropanes one of the directions of the reaction is the enlargement of the cyclopropane ring to the cyclobutane ring. Olefinic compounds are also formed by a mechanism similar to that for the α-halodialkylcyclopropanes.

EXPERIMENTAL

Tetrachloroneopentane [9]: Into a half-liter three-necked flask fitted with a reflux condenser and a stirrer was introduced 140 g PCl_5 and sulfur dioxide was passed through until the crystals disappeared completely. To the resultant mixture of $SOCl_2$ and $POCl_3$ was added 14 g pentaerythritol (0.1 mole); then under good stirring 8 g pyridine was added very slowly from a dropping funnel. With increasing evolution of heat the flask was cooled externally with iced water. The mixture was then gently boiled for 3 hours with stirring. This period sufficed for driving off the SO_2. After cooling, the flask contents were poured into iced water and stirred until the $POCl_3$ had been completely decomposed. The crystalline tetrachloroneopentane settled to the bottom and was collected by decantation or filtration. The product melted at 97° after recrystallization from alcohol, in agreement with the literature. Yield 21 g.

Tetrabromoneopentane was prepared from pentaerythritol and PBr_3 [10].

Tetraiodoneopentane was prepared from tetrabromoneopentane by the action of sodium iodide in methylethyl ketone [10]. The product melted rather lower than stated in the literature.

Dehalogenation of tetrachloroneopentane.

a) In aqueous alcohol. Into a flask were introduced 21 g tetrachloroneopentane, 50 ml alcohol, 17.5 ml water, 25 g zinc dust, 10.6 sodium carbonate and 2.5 g sodium iodide. The mixture was boiled. Formation of a hydrocarbon was not observed. The whole of the tetrachloro compound was recovered unchanged.

b) In ethylene glycol. The ratios of the reactants were the same as in a. Instead of aqueous alcohol, anhydrous ethylene glycol was used. Water was not added. The mixture was heated at 180-190°. 3 g of product distilled over. The product was distilled after washing with water and drying. The first drops came over at 40° and possessed a hydrocarbon odor. The main bulk came over at 80° and proved to consist of an unsaturated chloro compound. It was not investigated more closely.

c) In acetamide in presence of sodium carbonate. 21 g tetrachloroneopentane, 90 g anhydrous acetamide, 15 g sodium carbonate and 50 g zinc dust were put into a flask fitted with a stirrer and reflux condenser. The mixture was heated and intensively stirred. The reflux condenser was filled with warm water and connected through its upper end with a good cooling coil. Hydrocarbon began to form at 170-180°. Yield about 40%.

The hydrocarbon was washed with water, dried over calcium chloride and distilled over metallic sodium. The hydrocarbon began to boil at 33° but the main mass came over at 38-42°.

Raman spectrum: 305(2), 354(5), 373(3), 581(1), 613(1/2), 657(2), 779 (1), 872(3), 907(2), 957(10), 1033(1), 1150(1/2), 1191(2), 1393(2), 1428(3w), 1654(1/2), 1678(8), 2861(1), 2902 (4), 2921(4), 2952(5), 2989(8), 3069(3).

d) In acetamide in presence of sodium carbonate and sodium iodide. The experiment was performed as above. Supplementary addition of 5 g sodium iodide was made to the reaction mixture. Yield of hydrocarbon 45% of theory. B. p. 35-42.5°.

Raman spectrum: 305(2), 354(3), 375(2), 583(1), 613(1), 658(1), 777(1), 872(3), 905(2), 957(10), 1033(3), 1150(1), 1191(1), 1394(3), 1427(4w), 1654(2), 1679(5), 2828(1), 2857(1), 2902(2), 2923(2), 2951(3), 2988(6), 3065(4).

Dehalogenation of tetrabromoneopentane.

a) In aqueous alcohol. Experiments were performed in Gustavson's conditions. The results and the Raman spectroscopic data were presented in a previous paper [13].

b) In acetamide in presence of sodium carbonate. 38 g tetrabromoneopentane, 90 g anhydrous acetamide, 15 g sodium carbonate and 25 g zinc dust were used. The dehalogenation conditions were the same as in previous experiments. Hydrocarbon yield about 40% of theory. B. p. 35-42°.

Raman spectrum: 305(3), 353(2), 371(2), 581(1), 613(1), 657(1), 779(1), 873(3), 907(2), 957(10), 1032(3), 1150(1), 1191(1), 1394(3), 1429(4), 1654(2), 1679(5), 2829(1), 2861(1), 2900(2), 2921(2), 2947(2), 2989(5), 3070(3).

Dehalogenation of tetraiodoneopentane.

a) Zinc dust does not react with tetraiodoneopentane in aqueous alcohol.

b) In acetamide in presence of sodium carbonate and sodium iodide. 54 g tetraiodoneopentane, 90 g anhydrous acetamide, 15 g sodium carbonate, 5 g sodium iodide and 35 g zinc dust were taken. Reaction started at as low as 140-150°. Hydrocarbon yield about 80% of theory. B. P. 38-42°.

Raman spectrum: 305(3), 354(2), 374(2), 581(2), 613(1), 658(2), 777(1), 872(4), 905(2), 957(10), 1033(5), 1191(1), 1395(3), 1428(4 w), 1654(1), 1678(4), 2867(2), 2902(2), 2952(3), 2989(6), 3062(4).

c) In acetamide (without addition of sodium carbonate and iodide.) Conditions and quantities as in b). Reaction occurred at 160°. Yield about 80%. B. p. 36-42°.

Raman spectrum: 305(3), 354(2), 581(2), 613(1), 658(2), 779(4), 872(5), 905(1), 957(10), 1033(5), 1191(1), 1395(4), 1428(5 w), 1654(2–3), 1679(2–3), 2865(2), 2908(2), 2949(3), 2959(6), 3065(4).

SUMMARY

1. Zinc dust reacts with tetrahaloneopentanes in anhydrous acetamide to form a hydrocarbon mixture consisting of methylenecyclobutane, spiropentane and 2-methyl-1-butene.

2. The spiropentane content of this mixture increases in passage from tetrachloroneopentane to tetraiodoneopentane. Tetrabromoneopentane occupies an intermediate position.

3. Yields of spiropentane from tetraiodoneopentane do not change when sodium carbonate is present; this fact confirms its role as a means for regeneration of the iodine ion.

4. It is suggested that the rising yield of spiropentane in the order tetrachloroneopentane-tetrabromoneopentane-tetraiodoneopentane is related to the magnitude of the atomic radii of the halogens.

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MONOVINYLACETYLENE HOMOLOGS

II. ADDITION OF METHYL ALCOHOL TO Δ_1-CYCLOPENTENYL-ACETYLENE

I. A. Favorskaya and L. V. Fedorova

The present investigation was undertaken with the aim of studying the order of addition of methyl alcohol to the monovinylacetylene hydrocarbon series containing an endocyclic double bond. Particular interest is attached to the product of addition of one molecule of methyl alcohol to Δ_1-cyclopentenylacetylene in the 1,2-position, i.e., at the triple bond. Dienic ethers of the general formula $C_nH_{2n-4}O$, i.e., ethers in which one of the conjugated double bonds is in a five- or six-membered ring, have not previously been investigated. Nevertheless these compounds are of undoubted interest since we can use them, via the diene synthesis, for the preparation of diverse derivatives of bicyclic ketones of the decalone and hexahydroindanone series.

The experimental material relating to the addition to hydrocarbons containing adjacent double and triple bonds concerns mainly their simplest representative – monovinylacetylene. Work with this hydrocarbon has shown that addition may proceed in the 1,4-position or at the triple bond in the 1,2-position. In isolated cases the addition apparently takes place at the double bond.

The study of the order of addition of various reagents to systems containing a double and a triple bond is complicated by a series of secondary reactions which are made possible by the isomerizing tendency of the initially formed products with an allenic structure. Depending on the conditions, the isomerization of allenic compounds may proceed either in the direction of formation of acetylenes or in that of formation of dienes.

Addition of various reagents to monovinylacetylene homologs leads mainly to products of apparent or actual addition at the triple bond.

Addition of HCl to the simplest homolog of vinylacetylene, isopropenylacetylene, was studied by A. E. Favorsky [1]. Addition at the triple bond led to formation of chlorisoprene. Carothers and Coffman [2] obtained the same results when performing the reaction in similar conditions.

Homologs of monovinylacetylene not containing acetylenic hydrogen, of the general formula $CH_2=CH-C\equiv C-R$ (where $R = CH_3$, C_2H_5 or C_4H_9), react with concentrated hydrochloric acid to give products of addition at the triple bond [3].

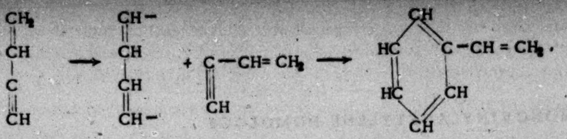
Carothers and Coffman [2] studied the reaction of sec. butenylacetylene and Δ_1-cyclohexenylacetylene with hydrochloric acid. On the analogy of the reaction with vinylacetylene itself, the authors assumed that addition took place at the 1,4-position with formation of the corresponding allenes. The latter undergo subsequent isomerization to diene derivatives, but since no intermediate products with an allenic structure were isolated, the reaction mechanism remained uncertain. Chlorides of similar structure may be obtained by addition of HCl at the triple bond.

A. I. Zakharova [4] studied the action of alcoholic alkali on sec. butenylacetylene; methyl alcohol added on at the triple bond.

The literature contains isolated facts, however, which confirm the susceptibility of vinylacetylene homologs to addition reactions in the 1,4-position. In an investigation of the addition of triphenylmethane to isopropenylacetylene, A. F. Thompson [5] obtained 1,1,1,6,6,6-hexaphenyl-2,3-hexadiene as the sole reaction product. Ozonolysis of the latter yielded triphenylacetic acid and 1,1,1-triphenyl-3-butanone.

Vinylacetylene homologs tend to dimerize in the same way as butadiene (Diels-Alder diene reaction). For the dimerization of vinylacetylene itself Dykstra [6] proposed a mechanism based on intermediate formation of an allenic structure due to addition in the 1,4-position.

According to A. E. Favorsky [7] the dimerization of monovinylacetylene in presence of methyl alcohol may be represented by the following scheme:



A similar mechanism was proposed by A. E. Favorsky and A. I. Zakharova [8] for the dimerization of isopropenylacetylene. It was shown that heating of isopropenylacetylene with methyl alcohol at 120° results in formation of 1-pseudobutenyl-3,4-dimethylbenzene in 50% yield.

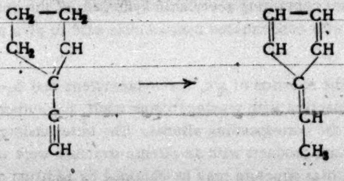
Our own observations indicate that dehydration of higher tertiary acetylenic alcohols over unburnt porcelain or $MgSO_4$ leads to formation of hydrocarbon dimers of the styrene type. The same observation was made by Shikhiev [9] on dehydration of methyl-n-propylethinyl carbinol. The yield of the dimer fraction of the hydrocarbon varies within wide limits depending on the structure of the carbinol undergoing dehydration. Thus, for example, in the dehydration of diisopropylethinyl carbinol, the dimer is the main reaction product (approx. 90%), whereas in the dehydration of α, α'-ethinylcyclopentanol a hydrocarbon dimer is not generally formed.

In this investigation of the addition of methyl alcohol to a monovinylacetylenic hydrocarbon containing an endocyclic double bond, the starting material was the Δ_1-cyclopentenylacetylene previously prepared by us.

It has been noted [10] that cyclopentenylacetylene possesses a yellow color which cannot be accounted for by its established structure. In order to clarify this problem, the hydrocarbon was purified via the copper derivative. The hydrocarbon regenerated from the copper derivative was colorless. Nevertheless the constants of the purified, colorless hydrocarbon almost coincided with those of the yellow hydrocarbon. The color was evidently due to the presence of traces of impurities which did not modify the constants.

On plotting the ultraviolet absorption spectra with a SP-22 spectrophotometer, using a cell of variable thickness, it was established that the yellow hydrocarbon has an absorption maximum at a wavelength of λ2800 3645 A. The absorption spectrum of dimethylfulvene contains three fairly strong bands at 2300, 2700 and 3650 A [11]. There are no experimental data in the literature for the spectrum of fulvene itself; however, we may assume that in the present case substitution has no influence on the absorption spectrum since it is known that the electron spectrum in the ultraviolet region is caused by conjugated double bonds.

On the basis, therefore, of the spectroscopic investigation of colored cyclopentenylacetylene, we established that it is contaminated with methylfulvene



The methylfulvene content of the mixture was determined by the oxidation method. It was found that the content of oxalic and acetic acids in the oxidation products only amounts to a few percent. After our paper [10] had gone to press a paper was published by Heilbron [12] which reported the preparation of Δ_1-cyclopentenylacetylene by dehydration of α, α'-ethinylcyclopentanol over aluminum phosphate. According to Heilbron, Δ_1-cyclopentenylacetylene is a faint-yellow liquid with a λ_{max} at 2270 A.

Addition of methyl alcohol to Δ_1-cyclopentenylacetylene was effected by us in presence of BF_3 and HgO.

Hennion and Nieuwland [13] added methyl alcohol to monovinylacetylene in presence of BF_3 and HgO. In these conditions additions of three molecules of methyl alcohol took place with formation of 2,2,4-trimethoxybutane. By analogy with Carother's results [14], the authors propose the following scheme:

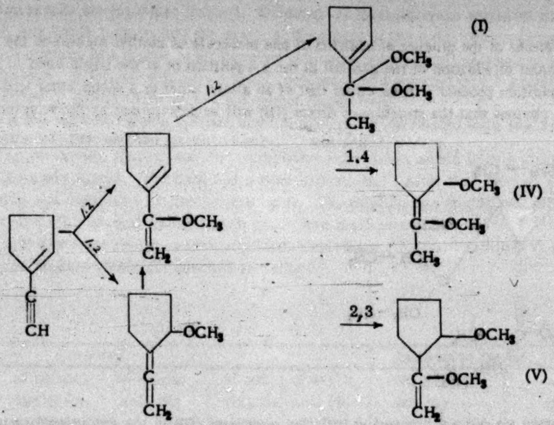
$$CH_2=CH-C\equiv CH \rightarrow CH_3OCH_2-CH=C=CH_2 \rightarrow$$

$$\rightarrow CH_3OCH_2-C\equiv C-CH_3 \rightarrow CH_3OCH_2-CH_2-C(OCH_3)_2-CH_3.$$

Since, however, no intermediate products were isolated the mechanism is still debatable.

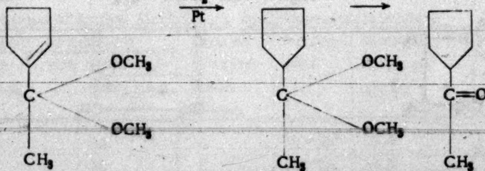
We isolated and characterized the following compounds as a result of reaction in the above-noted conditions of methyl alcohol with Δ_1-cyclopentenylacetylene: 2,2'-dimethoxy-2-Δ_1-cyclopentenylethane (I) -16%; 2,2'-dimethoxy-2-Δ_2-methoxycyclopentylethane (II) - 13 %; and the dimer $Cl_8H_{24}O_2$ (III) -45 %.

Addition of two molecules of methyl alcohol to Δ_1-cyclopentenylacetylene may proceed according to the scheme:


(I)
1.2
OCH₃
C
OCH₃
CH₃
1.2
1.2
C
CH
C—OCH₃
CH₂
OCH₃
C
CH₂
1,4
—OCH₃
(IV)
C—OCH₃
CH₃
2,3
OCH₃
C—OCH₃
(V)
CH₂

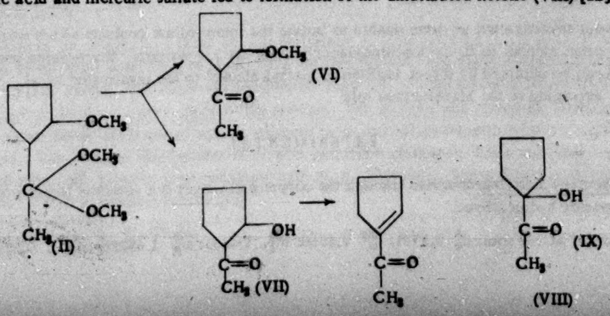
Depending on the order of addition of the alcohol to the hydrocarbon, the dimethoxy derivative of the hydrocarbon may have the structure corresponding to formulas (I), (IV) or (V).

The structure of the product of addition of two molecules of alcohol was established by hydrogenation and by hydrolysis in presence of dilute hydrochloric acid. Hydrolysis of the hydrogenation product yielded methylcyclopentyl ketone.


H₂
Pt
OCH₃
C
OCH₃
CH₃
OCH₃
C
OCH₃
CH₃
C=O
CH₃

On the basis of this observation we may say that the product of addition of two molecules of the alcohol to Δ_1-cyclopentenylacetylene has a ketal structure and corresponds to formula (I).

The structure of product (II) was established in the following manner: Hydrolysis in the cold in presence of dilute hydrochloric acid yielded 1-methoxy-2-acetylcyclopentane (VI). Hydrolysis of (II) by heating to 80° in presence of sulfuric acid and mercuric sulfate led to formation of the unsaturated ketone (VIII) [12].

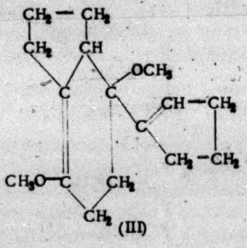

OCH₃
(VI)
C=O
CH₃
OCH₃
OCH₃
C
OCH₃
CH₃ (II)
OH
C=O
CH₃ (VII)
C=O
CH₃
OH
C=O
(IX)
CH₃
(VIII)

The intermediately formed β-ketoalcohol (VII) is unstable and splits off water to form the unsaturated ketone (VIII).

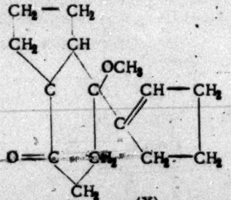
In these conditions the isomeric α-ketoalcohol, 1-hydroxy-1-acetylcyclopentane (IX) is perfectly stable and does not form the unsaturated ketone.

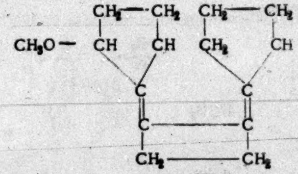
On the basis of these data we may say that the structure of (II) corresponds to 2,2'-dimethoxy-2-Δ_2-methoxy-cyclopentylethane.

Compound (III) is the dimer of the product of addition of one molecule of methyl alcohol to the hydrocarbon. Depending upon the order of addition of the alcohol in the 1,4-position or at the triple bond in the 1,2-position, the structure of the addition product will be either that of an allene ether or a diene ether with conjugated double bonds. It is quite obvious that the structure of dimer (III) will be determined by the structure of the monomeric ether


(III)

In the present investigation we did not succeed in isolating compound (III) in the analytically pure form in spite of repeated distillation at 0.1 mm. By hydrolyzing compound (III) in presence of dilute hydrochloric acid we obtained product (X), $C_{15}H_{22}O_2$, which contained only one methoxyl group, did not contain a hydroxyl group, and formed a semicarbazone. On the basis of these facts we attribute the structure 7-methoxy-7-Δ_1-cyclopentenylhexahydroindanone-4 (X) to the product of hydrolysis


(X)


(XI)

A similar ketone may be obtained by hydrolysis of the dimer which contains two nonequivalent methoxyl groups. Consequently the most probable formula for the structure of the dimer is (III) – 7-methoxy-7-Δ_1-cyclopentenyl-5,6,7,8-tetrahydroindane.

The tetrahydroindane (III) is formed by diene condensation of the monomeric diene ether. Compound (III) is not the dimer of the allenic ether (1,4 addition) since ketone (X) cannot be formed by hydrolysis of the dimer of structure (XI).

Hence in our investigation we were unable to isolate the intermediate products which would have confirmed the addition of methyl alcohol to Δ_1-cyclopentenylacetylene in the 1,4-position. The isolated products of the reaction (I and III) can be obtained by direct addition of methyl alcohol to the unsaturated ketal, which addition does not proceed according to the Markovnikov rule.

EXPERIMENTAL

Δ_1-Cyclopentenylacetylene (purified through the copper derivative) is a colorless liquid with the characteristic odor of acetylenic hydrocarbons:

B. p. 57.5-58° at 100 mm; d_4^0 0.8731; d_4^{20} 0.8596; n_D^{20} 1.4891; n_α^{17} 1.48825; n_β^{17} 1.50322; MR_D 30.94; calculated 29.86

0.1235 g substance: 0,4119 g CO_2; 0.0954 g H_2O. Found %: C 90.96; H 8.65. Calculated %: C 91,24; H 8.76.

For the constants of the unpurified methylfulvene-containing hydrocarbon, see [10].

Oxidation of yellow, methylfulvene-containing cyclopentenylacetylene. 20 g of hydrocarbon was taken for oxidation, which was effected by the normal method with the calculated amount of potassium permanganate. The oxidation results are set out in Table 1. Oxidation of methylfulvene would be expected to give acetic and oxalic acids, but Table 1 shows that the oxalic acid content of the oxidation products does not exceed 2-3%. The volatile acids contain 96% formic acid; therefore not more than a small percentage of acetic acid could also have been formed. It follows that only a small percentage of methylfulvene is present in the mixture.

Addition of Methyl Alcohol to Cyclopentenylacetylene.

1.5 g red HgO, 0.7 g $BF_3(C_2H_5)$ 20 and 0.5 ml CH_3OH was heated for a few minutes at 50-60°. A small quantity of the alcohol (about 10 ml) was added to the catalyst. The remaining alcohol and the hydrocarbon were slowly added from a dropping funnel. The reaction mass was vigorously stirred. The flask was cooled with water. After the whole of the hydrocarbon had been added, stirring was continued for another few hours. The solution was neutralized with sodium methylate and the alcohol distilled off. Several fractionations gave three main reaction products: 2,2'-dimethoxy-2-Δ_1-cyclopentenylethane (I), 2,2'-dimethoxy-2-Δ_2- methoxycyclopentenylethane (II), and the dimer $C_{16}H_{24}O_2$ (III). The experimental conditions and product yields are detailed in Table 2.

TABLE 1

Amount					Analysis of Ca salt of oxalic acid		
of hydrocarbon oxidized (g)	of normal NaOH for titration of volatile acids (in ml)	of formic acid (%)	of nonvolatile acids (%)	of oxalic acid (%)	wt. of Ca salt (g)	wt. of CaO (g)	% Ca found*
20	114.3	96.0	14.85	2.7	0.1380	0.0525	27.1
					0.1447	0.0560	27.6

TABLE 2

Reaction of Methyl Alcohol with Δ_1-Cyclopentenylacetylene

No.	Amount of reactants		duration of experiments (hours)	temperature	dimethoxy deriv. (I) (in %)	trimethoxy deriv. (II) (in %)	Dimer $C_{16}H_{24}O_2$ (III) (in %)
	hydrocarbon (in g)	methyl alcohol (in g)					
1	24	24	6	20–23°	15.6	13	43.7
2	15	30	6	25–26	15.8	12.4	45

Investigation of the Product of Addition of Two Molecules of Methyl Alcohol to Δ_1-Cyclopentenylacetylene (I)

B. p. 71-72° at 17 mm; d_4^{0} 0.9638; d_4^{20} 0.9467; n_D^{20} 1.4503; MR_D 44.39; calculated 44.18

0.1066 g substance: 0.2718 g CO_2; 0.0960 g H_2O; 0.1110 g substance; 0.2813 g CH_2; 0.0995 g H_2O; 0.1336 g substance; 19.82 g C_6H_6: Δt 0.211°. Found %: C 69.53, 69.11; H 10.08, 10.03; M 148.2. $C_9H_{16}O_2$. Calculated % C 69.24; H 10.26; M 156.2.

Hydrogenation of the unsaturated ketal (I) was performed in ether solution in presence of platinum black. 4.15 g substance in 30 ml ether with 0.3 g Pt black. The theoretical hydrogen requirement was 594.5 ml, whereas 660 ml was taken up (i.e. 110%). The ether was distilled off from the hydrogenation product, after which 14 ml water and 0.5 ml hydrochloric acid were added to the residue. The mixture was stirred at room temperature for 1.5 hours. The upper layer was removed and the aqueous layer was saturated with potassium carbonate and extracted with ether. The ethereal solution was dried with potassium carbonate. 2.2 g substance was obtained with b. p. 94-95° at 105 mm., n_D^{20} 1.4425; semicarbazone with m. p. 143-145°. These data are in accord with those in the literature for methylcyclopentyl ketone [15].

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* $C_2H_4Ca \cdot H_2O$. Calculated %: Ca 27.44.

Investigation of the Product of Addition of Three Molecules of Methyl Alcohol to Δ_1-Cyclopentenylacetylene (II)

B. p. 66-67° at 3 mm; n_D^{20} 1.4465; d_4^0 0.9999; d_4^{20} 0.9840; MR_D 51.096; calculated 51.10

0.1306 g substance: 0.3062 g CO_2; 0.1225 g H_2O. 0.1028 g substance: 0.2408 g CO_2; 0.0958 g H_2O. 0.1352 g substance; 18.78 g C_6H_6 Δt 0.20°. Found %: C 63.94, 63.88; H 10.49, 10.43; M 186.5. $C_{10}H_{20}O_3$. Calculated %: C 33.83; H 10.65; M 188.36.

Hydrolysis of product (II).

1) 3.5 g substance and 9 ml water with 3-4 drops hydrochloric acid were stirred at room temperature for 1.5 hours. The product was neutralized with potassium carbonate, salted out and dried over calcined K_2CO_3. Substance (VI), 1-methoxy-2-acetylcyclopentane, was obtained with b. p. 131-132° at 140 mm. Yield 2 g.

B. p. 114-115° at 72 mm; $n_D^{19.5}$ 1.4485; d_4^0 1.0009; $d_4^{19.5}$ 0.9851; MR_D 38.65; calculated 38.598.

0.0995 g substance: 0.2463 g CO_2; 0.0850 g H_2O. 0.0566 g substance: 0.1403 g CO_2; 0.0503 g H_2O. 0.1330 g substance; 18.92 g C_6H_6: Δt 0.27°. 0.0170 g substance: 7 ml 0.1N $Na_2S_2O_3$. Found %: C 67.54, 67.63; H 9.55, 9.94. M 134.9; OCH_3 21.28. $C_8H_{14}O_2$. Calculated %: C 67.54; H 9.93; M 142.19; OCH_3 21.83.

2) 5 g substance (II) was heated with vigorous stirring on the water bath for 1.5 hours with 25 ml 10% H_2SO_4 and a few crystals of $HgSO_4$. After cooling the reaction mass was neutralized and extracted with ether. The ethereal solution was dried with potassium carbonate. 3.5 g of substance (VIII) was obtained with b. p. 68-70° at 16 mm. Semicarbazone m. p. 204°. No depression in melting point resulted when mixed with the semicarbazone of 1-acetylcyclopentene-1 obtained by hydration of Δ_1-cyclopentenylacetylene.

Hydration of cyclopentenylacetylene. To a mixture consisting of 0.6 g H_2SO_4, 0.6 g $HgSO_4$ and 45 ml 70% aqueous methyl alcohol was slowly added dropwise 13 g of the hydrocarbon. Addition was effected at such speed that the temperature in the reaction flask did not rise above 50-55°. At the conclusion of the reaction the mixture was poured into a solution of sodium carbonate containing ether. The ethereal solution of the ketone was dried over calcined potassium carbonate. After distilling off the ether and methyl alcohol, the ketone (VIII) was distilled in vacuum. Yield 52.8% of theory.

B. p. 61-61.5° at 12 mm; 54° at 8 mm; n_D^{16} 1.4824; d_4^0 0.9712; d_4^{16} 0.9586; MR_D 32.78; calculated 31.87.

0.0936 g substance: 0.2612 g CO_2; 0.0770 g H_2O. 0.1577 g substance: 15.72 g C_6H_6: Δt 0.47°. Found %: C 76.12; H 9.20; M 110.5; $C_7H_{10}O$. Calculated %: C 76.32; H 9.15; M 110.15.

The semicarbazone of 1-acetylcyclopentene-1* was prepared. Its. m. p. after two recrystallizations from alcohol was 206-208°.

0.0934 g substance: 20.6 ml N_2 (771.3 mm, 23°). Found %: N 25.1 $C_8H_{13}ON_3$. Calculated %: N 25.13.

Hydration of α,α'-ethinylcyclopentanol. To a mixture of 0.6 g H_2SO_4, 0.6 g $HgSO_4$ and 45 g 70% aqueous methanol was added 15 g of the carbinol. The mixture was heated to 70° and stirred for 2 hours. The reaction products were worked up as in the case of hydration of α-α'-cyclopentenylacetylene. 12.5 g α-ketoalcohol (IX) was obtained (yield 71%).

B. p. 73-73.5° at 8 mm; n_D^{14} 1.4645; n_D^{20} 1.4642; d_4^0 1.0487; d_4^{20} 1.0323; MR_D 33.83; calculated 33.86.

0.1527 g substance: 0.3666 g CO_2; 0.1250 g H_2O. 0.2836 g substance; 15.66 g C_6H_6: Δt 0.71°. 0.0902 g substance: 15.66 g C_6H_6: Δt 0.24°. Found %: C 65.46; H 9.16; M 132, 124. $C_7H_{12}O_2$. Calculated %: C 65.59; H 9.43; M 128.12.

The semicarbazone was prepared and melted at 174-175° after recrystallization from alcohol.

Investigation of Dimer (III)

B. p. 138-140° at 1.5 mm; n_D^{23} 1.5150.

0.1198 g substance: 0.3335 g CO_2; 0.1028 g H_2O. 0.0855 g substance: 0.2378 g CO_2; 0.0756 g H_2O. 0.1575 g substance: 16.51 g C_6H_6: Δt 0.19°. 0.1914 g substance: 16.63 g C_6H_6: Δt 0.24°. 0.0236 g substance: 10.6 ml 0.1 . $Na_2S_2O_3$. Found %: C 75.92, 75.85; H 9.60, 9.89; M 260, 248.4; OCH_3 23.20; $C_{16}H_{24}O_2$. Calculated %: C 77.37; H 9.7; M 248.3; OCH_3 25.0

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* 1-Acetylcyclopentene-1 was prepared [12] by boiling Δ_1-cyclopentenylacetylene with 90% formic acid. The constants of the ketone deviate slightly from our data.

Hydrolysis of the dimer. 3.5 g dimer was energetically stirred at room temperature with 25 ml ethyl alcohol, 8 ml water and 1.5 ml HCl for 3 hours. The mixture was salted out with potassium carbonate, extracted with ether and dried with K_2CO_3. 2.2 g of product (X) was obtained with b. p. 130-134° at 1 mm; b. p. 94-96° at 0.1 mm, n_D^{22} 1.5190.

0.0784 g substance: 0.2197 g CO_2; 0.0659 g H_2O. 0.0749 g substance: 0.2103 g CO_2; 0.0631 g H_2O. 0.1325 g substance: 18.84 g C_6H_6: Δt 0.16°. 0.0190 g substance: 4.1 ml 0.1 $Na_2S_2O_3$. 0.0246 g substance: 5.7 ml 0.1 N $Na_2S_2O_3$. Found %: C 76.51, 76.57; H 9.42, 9.43; M 227.8; OCH_3 11.15, 11.16. $C_{15}H_{22}O_2$. Calculated %: C 76.89; H 9.46; M 234; OCH_3 13.25.

The semicarbazone was prepared and recrystallized from alcohol; m. p. 230-235° with decomposition. Test for hydroxyl groups was negative.

SUMMARY

1. Methyl alcohol reacts with Δ_1-cyclopentenylacetylene in presence of boron trifluoride and mercuric oxide with simultaneous addition of one, two and three molecules of the alcohol.

2. The product of addition of one molecule of the alcohol is converted in the reaction conditions into the dimer $C_{16}H_{24}O_2$, which on hydrolysis in an acid medium is transformed in turn into a ketone – 7-methoxy-7-Δ_1-cyclopentenylhexahydroindanone-4.

3. Addition of two molecules of methyl-alcohol to Δ_1-cyclopentenylacetylene takes place at the triple bond with the formation of an unsaturated ketal.

4. The product of addition of three molecules of methyl alcohol to the hydrocarbon corresponds in structure to 2,2'-dimethoxy-2-Δ_1-methoxycyclopentylethane.

5. It is shown that the yellow color of Δ_1-cyclopentenylacetylene is due to a trace of methylfulvene.

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* See Consultants Bureau translation, p. 701.

DECOMPOSITION OF BENZOYL PEROXIDE IN A MEDIUM OF SOME VINYL COMPOUNDS

M. F. Shostakovsky, E. P. Gracheva and V. A. Neterman

Investigation of the decomposition of benzoyl peroxide in a medium of vinyl compounds has great practical and theoretical interest [1-6]. In the study of polymerization processes great interest attaches to clarification of the role of peroxides and to the character of their decomposition during reaction with vinyl compounds. As we know [7], benzoyl peroxide and hydrogen peroxide sometimes decompose according to the scheme:

$$(C_6H_5CO)_2O_2 \rightarrow (C_6H_5CO)_2O + O;$$

$$H_2O_2 \rightarrow H_2O + O.$$

It is also known [8] that benzoyl peroxide decomposes according to the following schemes when heated or exposed to light rays:

$$(C_6H_5CO)_2O_2 \rightarrow C_6H_5-C_6H_5 + 2CO_2;$$

$$(C_6H_5CO)_2O_2 \rightarrow C_6H_5-COO-C_6H_5 + CO_2.$$

The decomposition of benzoyl peroxide is much more complicated in various solvents. In this case free radicals are formed:

$$(C_6H_5CO)_2O_2 \rightarrow C_6H_5 + C_6H_5COO' + CO_2,$$

$$C_6H_5COO' \rightarrow C_6H_5' + CO_2.$$

A series of products may be formed as a result of reaction of the free radicals with the solvent [9-11]:

$$C_6H_5' + C_6H_5Cl \rightarrow C_6H_5-C_6H_4Cl + H';$$

$$C_6H_5' + ROH \rightarrow C_6H_5-H + RO'$$

$$\text{or } C_6H_5' + H';$$

$$C_6H_5COO' + C_6H_5Cl \rightarrow C_6H_5COOH + C_6H_4Cl'.$$

According to the literature, therefore, the decomposition of benzoyl peroxide may proceed either with release of oxygen [12-15] or with formation of free radicals, e.g., phenyl and benzoate radicals [16-19].

In the course of a study of polymerization processes it was important to establish the possibility of breakdown of peroxides by a mechanism involving oxidation. Bearing in mind that the literature [9] does not consider all the conditions, in particular, of polymerization processes, we decided that a closer investigation of the mechanism of decomposition of peroxides in a series of reactions was necessary.

The induction process proceeds through formation of intermediate peroxy compounds. The proposals of Gelissen and Hermans [10] and of a number of other workers [20,21] on the course of decomposition of benzoyl peroxide apply only in presence of saturated and inert solvents and are directly related to the polymerization reaction.

The present authors have studied the decomposition of benzoyl peroxide in a medium of vinyl acetate methyl methacrylate, styrene and vinyl ethers. Peroxides were used both in small and relatively large amounts in order to effect a more detailed investigation of the decomposition products. The purpose of introduction of large amounts of benzoyl peroxide into the process was to isolate the products which form free radicals during conversion and dimerization. The very first experiments showed that in presence of a large excess of benzoyl peroxide, the polymerization reaction starts remarkably quickly and leads to formation of a polymer enclosing particles of peroxide. In order to avoid this behavior, an inert solvent (petroleum ether) was utilized. The solvent appreciably reduced the speed of polymerization, which permitted degrees of decomposition of benzoyl peroxide of up to

90% to be attained. These conditions fully permitted the investigation of peroxide-breakdown products. In Table 1 are presented the results of a study of the process of decomposition of benzoyl peroxide in a series of vinyl compounds.

TABLE 1

Products of Decomposition of Benzoyl Peroxide in Vinyl Compounds

No.	Used in reaction			Obtained in the reaction			Volume of O_2 obtained (ml)	% decomposition of peroxide with O_2 formation
	$(C_6H_5CO)_2O_2$ (g)	Compound	Weight (g)	O_2	CO_2	H_2O		
1	12.0	$CH_2=CHOCOCH_3$	72.1	0.7480	0.0384	0.0366	523.5	94.33
2	12.0	$CH_2=\overset{CH_3}{C}\ COOCH_3$	100.1	0.4043	0.0171	0.0542	282.94	51.0
3	12.0	$C_6H_5CH=CH_2$	104.1	–	0.0738	–	–	–

In these experiments (as well as in others) crystalline and gaseous products formed during benzoyl peroxide decomposition were isolated.

One of these products was benzoic acid. This provides conclusive evidence of symmetrical decomposition according to the scheme: $(C_6H_5CO)_2O_2 \rightarrow 2C_6H_5COO$. Diphenyl and phenyl benzoate were not detected among the reaction products.

EXPERIMENTAL

(Experimental data of V. P. Shishkova)

1. Decomposition of benzoyl peroxide in a medium of vinyl acetate. The main part of the apparatus for study of decomposition of benzoyl peroxide is a three-necked flask of 800 ml capacity. The central neck is connected to a reflux condenser. One of the other openings serves for a thermometer and the other for insertion of a tube through which nitrogen is bubbled. The nitrogen from a gasholder contains 0.5% oxygen and is passed through a system of Drechsler and Liebig bulbs for absorption of the oxygen, carbon dioxide and water. Directly attached to the reductor are two bottles filled with alkaline pyrogallol solution for absorption of the oxygen. The nitrogen then flows through sulfuric acid, two towers containing soda lime and one tower containing $CaCl_2$ and then through a cotton wool filter. In front of the reaction flask is a three-way piece with one limb connected to a mercury manometer for regulating the gas pressure in the system. From the cotton wool filter the nitrogen (now pure and dry) passes into the reaction flask via a bubbler.

The top of the reflux condenser is connected to a system of absorption vessels in the following order (of gas flow): A buffer vessel to receive any reaction mass or condensate ejected through the reflux condenser, a U-tube containing $CaCl_2$ for absorption of H_2O, two coil-shaped traps cooled to −45 degrees with solid carbon dioxide and acetone, an Ivitsky-type bottle containing aqueous $Ca(OH)_2$, a U-tube containing active carbon for absorption of traces of organic matter not retained in the cooled traps, two U-tubes containing soda lime for absorbing CO_2.

All of the gases evolved in the reaction are driven out with nitrogen and pass through the absorption system before being collected in a gasholder over a saturated aqueous solution of sodium chloride. The amount of oxygen was determined by absorption with alkaline pyrogallol in a "TI-4" apparatus.

Substances used in reactions had the following constants: 1) Vinyl acetate, b. p. 71.5-71.9° (737.4 mm); n_D^{20} 1.3960; 2) petroleum ether, b. p. 80-107°; n_D^{20} 1.4139; 3) benzoyl peroxide, prepared by two recrystallizations from absolute diethyl ether, m. p. 102.7-103.0°.

Into the reaction flask of the above-described apparatus were introduced 72.12 g vinyl acetate, 12.0 g benzoyl peroxide and 120.03 g petroleum ether. The system was filled with pure, dry nitrogen. The temperature of the reaction medium was gradually raised to 86°. The maximum temperature during an experiment was 87.5°. At the end of the first hour, at a temperature of about 53°, the whole of the benzoyl peroxide had dissolved and evolution of fine gas bubbles which rose up was observed. At 70° the mass was observed to boil and condensate at times filled part of the lower bulb of the reflux condenser. The temperature was maintained for 3 hours at 70-86°, after which the reaction flask was cooled while a nitrogen stream was continuously passed through the system. The pressure during an experiment was 18-20 mm. The total duration of an experiment was 5 hours. During a reaction 5000 ml gas containing 10.47 vol % oxygen was collected in the gasholder, the amount being converted to normal temperature and pressure (Table 2).

Thus 94.3% (11.32 g) of the benzoyl peroxide introduced was decomposed with evolution of oxygen. Assuming that CO_2 also originated from decomposition of peroxide, we must assume that 1.76% of the original benzoyl peroxide decomposed to give CO_2.

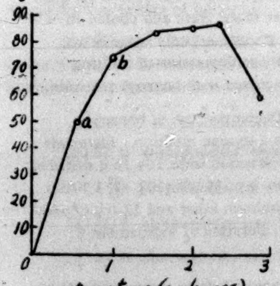
TABLE 2

Taken	g	Obtained	g
$CH_2=CHOCOCH_3$	72.12	Solution of polymer in petroleum ether	107.87
$(C_6H_5CO)_2O_2$	12.00	Crude polymer	91.62
Petroleum ether	120.03	CO_2	0.0384
Total	204.15	O_2	0.7480
		Condensate in trap	1.90
		H_2O	0.0366
		Tube containing active carbon	0.1676
		Total	202.3806

A second possible source of the CO_2 is oxidative decomposition of the starting substances, principally vinyl acetate. This possibility is supported by the fact that the following amount of water was formed during the reaction: a) found 0.0366 g; b) calculated from the CO_2 assuming complete oxidation to H_2O and CO_2, 0.012 g, i.e., the water found was three times as much as would correspond to the amount of CO_2 found whose absorption cannot be quantitiative due to the high velocity of the nitrogen stream.*

In addition to the gaseous reaction products great interest attaches to the products formed directly in the reaction flask. The reaction yielded a polymer which settled out in the form of a viscous, resinous mass, and an upper layer comprising a solution of individual reaction products in petroleum ether. The total quantity of reaction mixture was 199.49 g, from which were isolated 91.62 g "crude polymer" and 107.87 g solution with a marked odor of petroleum ether and a faint odor of vinyl acetate.

The "crude polymer" was dissolved in acetone by heating on the water bath and was treated with 71.5 ml 5% aqueous KOH. A polymer was thus obtained in the form of a white, curd-like mass, and the aqueous acetone alkaline solution containing potassium benzoate was separated. The acid was isolated by treating the residue after evaporation with H_2SO_4 and repeatedly crystallizing it from water. Benzoic acid was identified by the m. p. of 121.5° and by the m.p. of 120.8° of the mixed sample.



From the petroleum ether solution after supplementary freezing at −60° was isolated a further 2.4 g polyvinyl acetate; after this the total solution (101.3 g with n_D^{20} 1.4151) was fractionated to give the following fractions: 1) b. p. 76-85.8° 17.37 g, n_D^{20} 1.4128; 2) b.p. 85.8-102.5°, 77.62 g, n_D^{20} 1.4120; 3) flask residue 4.43 g.

The second fraction was refractionated: 1) b. p. 77-85.5° 9.81 g, n_D^{20} 1.4158; 2) b. p. 85.5-94° 62.36 g, n_D^{20} 1.4135; 3) flask residue 2.90 g, n_D^{20} 1.4154.

The residues from both fractionations were combined and refractionated: 1) b. p. 50-93° 3.91 g; 2) b. p. 50-70° (11 mm) 0.33 g; 3) residue 2.60 g.

The first fraction (3.91 g) obtained by fractionation of the residues was again fractionated: 1) b. p. 65-85° 0.68 g, n_D^{20} 1.4084; 2) b. p. 85-102° 2.55 g, n_D^{20} 1.4138; 3) residue 0.26 g, n_D^{20} 1.4140.

The first fraction had a sharp odor of acetic acid.

On fractionation of the products of reaction contained in the petroleum ether solution, in all the experiments white crystals of benzoic acid were deposited on the sides of the dephlegmator and the condenser (m. p. 121.5°).

Finally, the condensate in the CO_2-cooled trap was examined. In all 1.90 g of readily volatile liquid with a pungent odor was collected. It dissolved completely in water. The aqueous solution gave the characteristic reaction for acetaldehyde with fuchsine sulfuric acid.

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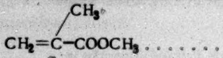
* The trap containing $Ca(OH)_2$ solution showed that carbon dioxide begins to come off immediately after solution of the whole of the benzoyl peroxide.

0.0786, 0.0613 g substance: 0.0035, 0.0030 g CH_3CHO (according to Ripper). Found %: CH_3CHO 4.45,4.89.

II. Decomposition of benzoyl peroxide in methyl methacrylate. Materials used: 1) methyl methacrylate, b. p. 24-31.5° (35-37 mm), n_D^{20} 1.4156; 2) petroleum ether, b. p. 80-107°, n_D^{20} 1.4139; 3) benzoyl peroxide, m. p. 102.7-103.0°.

The experiment was performed in the above-described apparatus but omitting the $Ca(OH)_2$ bottle. Into the reaction flask were charged 100.1 g methyl methacrylate, 120.1 g petroleum ether and 12.0 g benzoyl peroxide. The rate of heating of the reaction mixture is plotted in the diagram. The whole of the benzoyl peroxide had dissolved in about 40 minutes after the start of the reaction at a temperature of about 53°; gas bubbles appeared at the surface of the liquid which rapidly began to grow turbid. A white flocculent precipitate of polymethyl methacrylate settled to the bottom of the reactor; after 1.5 hours the solution was highly viscous and a solid mass of polymer was at the bottom. The total duration of the experiment was 2 hours 40 minutes; the maximum temperature during the experiment was 88°. A total of 5098 ml of gases was collected in the gasholder and the oxygen content was 5.55 vol.%. In the trap, cooled in a Dewar flask, was collected about 2 g substance with a sharp aldehydic odor, n_D^{20} 1.3940 (Table 3).

TABLE 3

Taken	g	Obtained	g
 $CH_2{=}\overset{CH_3}{C}{-}COOCH_3$	100.12	Solution	70.33
$(C_6H_5CO)_2O_2$	12.00	Polymer (crude)	157.27
Petroleum ether	120.07	CO_2	0.0171
		Tube containing active carbon	0.0567
Total	232.19	O_2	0.4043
		H_2O	0.0542
		Condensate in trap	1.97
		Total	230.1023

51% (6.1204 g) of the benzoyl peroxide used in the reaction was decomposed to oxygen but if we assume that the CO_2 originated from decomposition of peroxide then the amount of CO_2 found corresponds to 0.78% benzoyl peroxide. The amounts of water found and calculated (on the basis of the CO_2) are in close agreement: Found: 0.054 g, calculated from the CO_2: 0.056 g.

The upper layer was poured off from the polymer in the flask and cooled to −15° when 1.25 g white crystals came down. M.p. 100.5°; no depression of melting point when mixed with benzoyl peroxide.

TABLE 4

Taken	g	Obtained	g
$C_6H_5CH{=}CH_2$	104.14	Solution	232.80
$(C_6H_5CO)_2O_2$	12.0	Condensate	0.92
Petroleum ether	120.0	CO_2	0.0738
Total	236.14	Total	233.79

III. Decomposition of benzoyl peroxide in a styrene medium. Materials used in the reaction were 104.14 g distilled pure styrene, b.p. 34-35° [10], n_D^{20} 1.5462; 120.0 g petroleum ether and 12.0 g benzoyl peroxide. Duration of experiment 2 hours 17 minutes; maximum temperature 86.5°; total gas volume 3728 ml.

No oxygen was found on analysis of the collected gases. The absence of oxygen is fully understandable when we take into account the ease of oxidation of styrene [22].

The following observations were made in the reaction: 1) The weight of the tube with active carbon increased by 0.0028 g 2) the amount of condensate in the trap was 0.92 g, n_D^{20} 1.3880; 3) tube containing soda lime increased in weight by a) 0.0552 g, b) 0.0186 g.

In addition a solution of turbid, oily liquid was obtained with a predominant odor of petroleum ether. The weight of the solution was 232.80 g; n_D^{20} 1.4789. On standing the solution deposited a heavy, oily liquid in quantity of 1.9 g; n_D^{20} 1.3485 (Table 4).

On converting the quantity of evolved CO_2 to benzoyl peroxide we obtain a value of 3.38% for decomposition of the peroxide.

IV. Investigation of the reaction of vinyl-n-butyl ether with benzoyl peroxide. (Experimental work by E. P. Gracheva). 100 g vinylbutyl ether and 12 g benzoyl peroxide were placed in a round-bottomed flask fitted with a mechanical stirrer.

After heating for 38 hours the reaction mixture was fractionated: 1) b.p. 94° 97.7 g, n_D^{20} 1.4023, i.e. unchanged vinylbutyl ether; 2) b.p. 74-75° (12 mm) 4.7 g, n_D^{20} 1.4040, d_4^{20} 0.8260.

13.01 mg substance: 14.60 mg H_2O; 32.30 mg CO_2. 10.22 mg substance: 11.61 mg H_2O; 25.43 mg CO_2. Found %: C 67.75, 67.90; H 12.55, 12.71. $C_{10}H_{22}O_2$. Calculated %: C 68.4; H 12.9.

After taking off the above fractions the residue in the flask was a viscous mass (13.1 g). A part of the residue was treated with hot water, filtered from insoluble material and left to stand; large white crystals came down with m.p. 120-121°. Yield 3.75 g. A mixture with benzoic acid did not depress the melting point.

The residue on the filter was insoluble benzoyl peroxide (m.p. 102-103°) in amount of 4.21 g. The other portion of the residue (2.5 g) dissolved in benzene. The solution was saturated with dry ammonia; a voluminous precipitate was formed which was again filtered and subjected to a supplementary extraction with hot benzene. This treatment left a residue of 1.1 g ammonium benzoate on the filter; m.p. 180-181°. It did not depress the melting point of an authentic specimen.

SUMMARY

1. It is shown that in a medium of vinyl compounds benzoyl peroxide is mainly decomposed into benzoic acid and oxygen.

2. The $C_6H_5COO^{\cdot}$ or $CH_3COO^{\cdot}$ radicals may undergo secondary decomposition with loss of oxygen [13].

3. Peroxides are sources of both free radicals and oxygen, and the latter is a catalytic initiator of the free-radical chain reaction of polymerization.

4. Decomposition of benzoyl peroxide in a medium of a series of solvents with formation of free phenyl radicals and benzoate, as established by Gelissen and Hermans, cannot be regarded as the invariable type of reaction in all forms and conditions of processes of polymerization initiated by peroxide.

5. The scheme advanced by us for decomposition of peroxides is fully consistent with the polymerization conditions caused not only by radicals but also by atmospheric oxygen and is in complete accord with the mechanism of action of inhibitors.

6. Benzoyl peroxide does not promote the processes of polymerization of vinyl ethers, which fact is indirect proof of the correctness of our scheme for the decomposition of peroxides. This conclusion is fully consistent with the fact that oxygen does not promote the polymerization of vinylalkyl ethers.

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* See Consultants Bureau translation, p. 541.

ACETYLENIC ALCOHOLS AND GLYCOLS

I. SYNTHESIS AND TRANSFORMATIONS OF 1,4-BUTYNEDIOL

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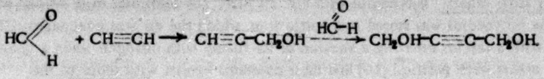
1,4-Butynediol is prepared by condensation of acetylene with formaldehyde [1,2]. Concerning the transformations of 1,4-butynediol we know that it can be brominated, forms a dimethyl ether [3], and adds on water [4] and hydrogen [5]. Diacetylene can be obtained by chlorination of butynediol followed by detachment of hydrogen chloride [6]. There are indications that pyrroles can be prepared from butynediol. Like acetylene, butynediol can be cyclized, forming hexamethylol benzene which can be oxidized to mellitic acid.

It appeared of interest to us to investigate the reaction of butynediol with vinyl ethers. Such an investigation was also expedient because the only compounds of butynediol containing ethereal groups mentioned in the literature are the dialkyl ethers (dialkoxybutynes). These are prepared by the action of chloromethylalkyl ethers on acetylene dimagnesium bromides [7].

Butynediol is synthesized from formaldehyde and acetylene under the influence of acetylides of metals according to the equation:

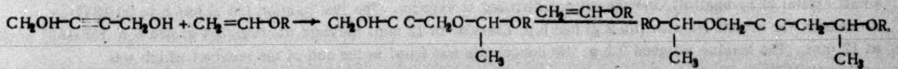


$$H\overset{O}{\underset{H}{C}} + CH\equiv CH \rightarrow CH\equiv C{-}CH_2OH \xrightarrow{H\overset{O}{C}{-}H} CH_2OH{-}C\equiv C{-}CH_2OH.$$

A study was made of the effect of temperature, pressure, duration of heating and type of catalyst on the course of this synthesis. We deviated from the literature procedure by not diluting the acetylene with nitrogen, thereby considerably simplifying the experimental technique and increasing the efficiency of the conversion.

With the aim of standardizing the preparative method we performed the synthesis of butynediol by the above-mentioned condensation [2] in an autoclave. Utilization of a catalyst supported on silica gel permits the yield of butynediol to be increased. One portion of catalyst can serve for ten consecutive charges of formaldehyde.

A study was made of the reactions of butynediol with vinylethyl and vinylbutyl ethers according to the scheme:



$$CH_2OH{-}C\equiv C{-}CH_2OH + CH_2{=}CH{-}OR \rightarrow CH_2OH{-}C\;\;C{-}CH_2O{-}\underset{CH_3}{\underset{|}{CH}}{-}OR \xrightarrow{CH_2=CH-OR} RO{-}\underset{CH_3}{\underset{|}{CH}}{-}OCH_2{-}C\;\;C{-}CH_2{-}\underset{CH_3}{\underset{|}{CH}}{-}OR.$$

This reaction was carried out both with a catalyst (traces of acid) and thermally without a catalyst [8].

The reaction yielded mono- and di-α-alkoxyethyl ethers of butynediol in the form of colorless, pleasant-smelling liquids soluble in organic solvents (the monoethers were difficultly soluble in benzene). All the investigated ethers decomposed when heated. Diethylacetal was isolated from the products of decomposition of the di-α-ethoxyethyl ether of butynediol. The di-α-ethoxy ethers were more stable than the corresponding di-α-butoxy ethers and they can be distilled at atmospheric pressure with only partial decomposition. The residues after fractionation of the α-alkoxyethyl ethers of butynediol are transparent, brown resins which decompose explosively when heated. The structure of the mono- and di-α-alkoxyethyl ethers of butynediol was established by hydrolysis [9]. We demonstrated the presence of a triple bond in the derived acetals by hydrogenating the di-α-butoxyethyl ether of butynediol over platinum oxide; the triple bond underwent exhaustive hydrogenation and the acetal was degraded.

Laboratory assistant M. S. Egorova participated in the experimental work.

EXPERIMENTAL

Preparation of 1,4-butynediol. Commercial 30% formalin and technical acetylene were utilized for the synthesis. Commercial reagents of the normal degree of purity were used in preparation of the catalyst.

The catalyst and 217 g formalin were charged into a 2.5 liter rotating autoclave equipped with a thermocouple. A stream of acetylene was passed through the autoclave to establish an acetylene pressure of 13-15 atm. The autoclave was rotated and heated to 97-105° in the course of one hour. After cooling and further addition of acetylene, heating was effected for another 3 hours. During this period 43-49 liters of acetylene was absorbed. After cooling, the autoclave was discharged, the liquid product being carefully decanted from the catalyst. 217 g formalin was added to the catalyst residue in the autoclave and the operation was repeated in the above manner. The discharged product was filtered through filter paper (220 ml filtrate); it consisted of a transparent, yellow liquid. The water was distilled off at 47-50 mm; the residue contained 69.5 g crystalline butynediol, m.p. 55-57°. Yield of technical product 80.8% of theory. Vacuum fractionation of 69.5 g of technical product gave 58.7 g with b.p. 151-152° at 23 mm and a residue of 9.1 g. The latter was a dark-colored resin soluble in water.

The prepared butynediol had b.p. 151-152° at 23 mm; 137-138° at 10 mm; m.p. 57-58°.

Literature data: b.p. 132-135° (5 mm); m.p. 55-58° [2].

15.14 mg substance: 30.85 mg CO_2; 9.41 mg H_2O. 15.47 mg substance: 31.53 mg CO_2; 9.84 mg H_2O. Found %: C 55.61, 55.62; H 6.95, 7.11. $C_4H_6O_2$. Calculated %: C 55.81; H 6.98.

The yield of pure butynediol was 68.3% of the theoretical.

Reaction of butynediol with vinyl ethers. Butynediol with b.p. 137-138° (10 mm) and m.p. 57-58° was used in all the transformations. The butynediol was stored in a bottle from which the air was evacuated. The stopper of this bottle was provided with a tap for creating a vacuum or for filling with nitrogen when a quantity was being weighed out. The vinyl ethers were purified [10] and their constants agreed with those in the literature. Vinylbutyl ether: b.p. 93.5-94°; n_D^{20} 1.4015; vinylethyl ether: b.p. 35.5-36°, n_D^{20} 1.3780.

The dioxane used was purified [11] and had b.p. 101-101.5°; freezing point 11.6°.

a) Catalytic reaction of butynediol with vinylethyl ether in dioxane solution. A solution of 43 g (0.5 mole) butynediol in 50 g dioxane, prepared at +40°, was placed in a three-necked flask fitted with thermometer, stirrer, dropping funnel and reflux condenser. A drop of concentrated hydrochloric acid was added while stirring, and addition was then made dropwise over a period of 3 hours of 75 g vinylethyl ether. During this stage the temperature of the reaction mixture was raised to 36-42°. Addition of the whole quantity of vinylethyl ether was followed by continued heating on the water bath at 48-50° for 2½ hours. The discharged product, a slightly colored liquid, was treated with powdered potassium carbonate and left over the latter overnight. It was filtered, 46.8 g dioxane was distilled off (in a stream of dry nitrogen and in presence of a small crystal of pyrogallol), and the residue distilled in vacuum. The first fraction (14 g) had b.p. 30-134° at 12 mm; the second fraction (89.2 g) had b.p. 134-138° at 12 mm; the third fraction (5.7 g) had b.p. 138-150° at 12 mm. The residue weighed 7.5 g. No condensate was found in the coil of the receiver which was cooled to −40°.

The first fraction was fractionated to remove the dioxane and then combined with the second fraction. Fractional vacuum distillation of the latter gave 88 g of material with the constants: b.p. 126-127° at 8 mm; 254-255° at 736 mm (with slight decomposition); n_D^{20} 1.4400; d_4^{20} 0.9749; MR_D 62.26; calculated 62.19.

0.2572 g substance: 15.81 g benzene: Δt 0.370°. 0.2338 g substance: 15.81 g benzene: Δt 0.340°. Found: M 225.1, 222.7. $C_{12}H_{22}O_4$. Calculated: M 230.29. 3.830 mg substance: 8.804 mg CO_2; 3.300 mg H_2O. 3.604 mg substance: 8.310 mg CO_2; 3.069 mg H_2O. Found %: C 62.72, 62.92; H 9.63, 9.52. $C_{12}H_{22}O_4$. Calculated %: C 62.57; H 9.63.

The isolated product is the di-α-ethoxyethyl ether of butynediol. Yield 76.5%.

b) Reaction of butynediol with vinylethyl ether in the autoclave without catalyst. 43 g butynediol and 75 g vinylethyl ether were introduced into a 0.5 liter autoclave. While rotating, the autoclave was heated to 88-96° in the course of 9 hours. After cooling, 112 g of clear liquid product was discharged and fractionated in vacuum: First fraction, b.p. up to 129° at 28 mm −10.5 g; second fraction, b.p. 129-131° at 28 mm −90.5 g; third fraction, b.p. 131-134° at 29 mm −2.0 g; residue 4.0 g. In the coil of the receiver, cooled to −40°, 4.0 g of condensate collected.

The first fraction was freed from low-boiling constituents by fractionation and then combined with the second fraction. The low-boiling portion of the first fraction was combined with the condensate in the receiver coil.

The second fraction was the di-α-ethoxyethyl ether of butynediol which had the following constants after fractionation: b.p. 128.0-129.0 at 9.5 mm; n_D^{20} 1.4400; d_4^{20} 0.9752. Yield 78.8% of theory.

Examination of the condensate in the coil of the receiver (cooled to −40°). The condensate contained traces of acetaldehyde (reaction with fuchsin-sulfurous acid). The condensate from this experiment was combined with the condensates from several similar experiments; repeated fractionation at atmospheric pressure then led to the isolation of diethylacetal with the constants: b.p. 102-103.5° (747 mm); n_D^{20} 1.3816; d_4^{20} 0.8295; MR_D 33.12; calculated 33.19.

Isolation of the diethylacetal in this case raises the question of the thermal decomposition of the prepared ethers of butynediol.

c) Preparation of the mono-α-ethoxyethyl ether of butynediol. In the conditions of the above-described experiment 43 g (0.5 mole) butynediol and 37 g (0.5 mole) vinylethyl ether were charged into the autoclave. The rotating autoclave was heated to 81-88° in the course of 1½ hours. After cooling, the clear product (74.5 g) was fractionated in vacuum: First fraction, b.p. 105-128° at 13 mm −9.8 g; second fraction, b.p. 128-129° at 13 mm −30.6 g; residue 29.4 g.

When the residue was cooled it deposited crystals of unchanged butynediol. These were separated from the liquid and weighed 18.9 g after washing with ether and drying in a vacuum desiccator. M.p. 56-57°. The coil of the receiver, cooled to −40°, was found to contain 4.0 g condensate.

The first fraction was divided between the coil condensate and the second fraction. After fractionation the second fraction had the following constants: b.p. 124-124.5° at 10 mm; n_D^{20} 1.4550; d_4^{20} 1.0192; MR_D 41.95; calculated 42.12.

3.580 mg substance: 8.019 mg CO_2; 2.820 mg H_2O. 3.355 mg substance: 7.510 mg CO_2; 2.700 mg H_2O. Found %: C 61.13, 61.09; H 8.81, 9.00. $C_8H_{14}O_3$. Calculated %: C 60.73; H 8.92.

The obtained data enable us to identify the product as the mono-α-ethoxyethyl ether of butynediol. Yield 69.1% of theory, calculated on the reacted butynediol.

d) Catalytic reaction of butynediol with vinylbutyl ether in dioxane solution. In the previously described conditions dropwise addition was made, with stirring, of 110 g vinylbutyl ether over a period of 1½ hours to a solution of 43 g butynediol in 50 g dioxane in presence of a drop of concentrated hydrochloric acid. The mixture was then heated to 40° in the course of 3 hours, and after cooling it was treated with potassium carbonate. 48 g dioxane was distilled off in a dry nitrogen stream. The residue was distilled in vacuum: First fraction, 40-117° at 15 mm −18.6 g; second fraction, 117-167° at 12 mm −5.0 g; third fraction, 167-170° at 12 mm −86.8 g; residue 18.6 g. 5 g liquid product collected in the coil receiver which was cooled to −40°.

From the first fraction was isolated 14 g dibutylacetal with b.p. 184.5-185°; n_D^{20} 1.4090; d_4^{20} 0.8280. These constants agree with the literature data [12,13].

Vacuum fractionation of the second and third fractions yielded 90.0 g of a product with the constants: b.p. 152-153° at 3 mm; n_D^{20} 1.4445; d_4^{20} 0.9355; MR_D 81.32; calculated 80.66.

0.2524 g substance: 13.09 g benzene: Δt 0.36°. 0.2394 g substance; 13.09 g benzene: Δt 0.34°. Found: M 274.25, 275.40. $C_{16}H_{30}O_4$. Calculated: M 286.40. 4.230 mg substance: 10.414 mg CO_2; 4.110 mg H_2O. 3.689 mg substance: 9.084 mg CO_2; 3.530 mg H_2O. Found %: C 67.22; 67.20; H 10.87, 10.70. $C_{16}H_{30}O_4$. Calculated %: C 67.10; H 10.56.

The isolated product is the di-α-butoxyethyl ether of butynediol. Yield 64.3% of the theoretical. The residue was brown, viscous liquid.

e) Reaction of butynediol with vinylbutyl ether in the autoclave without catalyst. 60 g (0.7 mole) butynediol and 150 g (1.5 moles) vinylbutyl ether were placed in a 0.5 liter rotating autoclave. The autoclave, while rotating, was heated to 96-110° in the course of 8½ hours. After cooling, the clear liquid product (192 g) was fractionated in vacuum in a stream of dry nitrogen in presence of a crystal of pyrogallol. First fraction, up to 85° at 18 mm, 11 g; second fraction, 85-147° at 18 mm, 6.5 g; third fraction, 147-156° at 18 mm, 28.5 g; fourth fraction, 156 167° at 18 mm, 64.5 g; fifth fraction, 167-170° at 18 mm, 49.0 g; residue 16.2 g. 10 g liquid was condensed in the coil receiver (cooled to −40°).

The first fraction gave a strong reaction for acetaldehyde with fuchsin-sulfurous acid. Butyl alcohol with the following constants was isolated from it by two fractionations: b.p. 117-118°; n_D^{20} 1.3990; d_4^{20} 0.8040.

Dibutylacetal with the following constants was separated from the second fraction: b.p. 185-185.5°; n_D^{20} 1.4095; d_4^{20} 0.8282. These values agree with the literature data [12-14].

The third fraction was butynediol, which crystallized in the receiver and had the following constants after distillation: b.p. 137-137.5° (9 mm); m.p. 57-58°.

On the following day 6 g crystalline butynediol was filtered off from the fourth fraction; two fractionations of the filtrate then gave 5 g of a product with the following constants: b.p. 121-122° (3 mm); n_D^{20} 1.4570; d_4^{20} 0.9745; MR_D 52.05; calculated 51.19.

0.2338 g substance; 18.81 g dioxane: Δt 0.33°. 0.1482 g substance; 18.81 g dioxane: Δt 0.215°. Found: M 188.38, 183.25. $C_{10}H_{18}O_3$. Calculated: M 186.244. 15.26 mg substance: 35.76 mg CO_2; 13.68 mg H_2O. 9.69 mg substance: 22.67 mg CO_2; 8.53 mg H_2O. Found %: C 63.95, 63.76; H 10.03, 9.84. $C_{10}H_{18}O_3$. Calculated %: C 64.49; H 9.74.

The isolated substance is the mono-α-butoxyethyl ether of butynediol.

The residue from the fourth fraction was combined with the fifth fraction and twice distilled in vacuum to give 51.0 g product with the following constants: b.p. 151-152° (2 mm); n_D^{20} 1.4440; d_4^{20} 0.9353; MR_D 81.32; calculated 80.60.

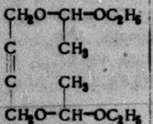
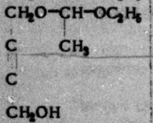
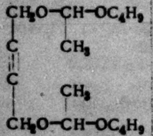
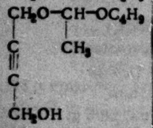
3.73 mg substance: 9.200 mg CO_2; 3.586 mg H_2O. 5.378 mg substance: 13.244 mg CO_2; 5.160 mg H_2O. Found %: C 67.31, 67.21; H 10.85, 10.83. $C_{16}H_{30}O_4$. Calculated %: C 67.10; H 10.56.

The isolated substance is the di-α-butoxyethyl ether of butynediol. Its yield is 60.2% of the theoretical based on the reacted butynediol. The residue is a resinous, transparent, viscous liquid.

f) Preparation of the mono-α-butoxyethyl ether of butynediol. 43 g (0.5 mole) butynediol and 50 g (0.5 mole) vinylbutyl ether were heated in an autoclave in the conditions of the preceding experiment to 96-104° in the course of 1½ hours. 89 g of clear product was discharged and after 3 hours this deposited crystalline butynediol (5 g). The filtrate was fractionated in vacuum: First fraction, 23-120° at 4 mm, 2.9 g; second fraction, 120-127° at 4 mm, 17.1 g; third fraction, 127-134° at 4 mm, 17.8 g; fourth fraction, 134-143° at 6 mm, 6.6 g; residue, 31.1 g (decomposition of the product commenced). Two fractionations of the first fraction yielded dibutylacetal with b.p. 183.5-184.5°; n_D^{20} 1.4085; d_4^{20} 0.8280. The second fraction was butynediol which crystallized in the receiver, m.p. 57-58°. From the third and fourth fractions were isolated 21.8 g mono-α-butoxyethyl ether of butynediol with b.p. 126-127° at 7 mm; n_D^{20} 1.4565; d_4^{20} 0.9750. Yield 38.0% of theory, based on the reacted butynediol.

Hydrolysis of the α-alkoxyethyl ethers of butynediol. Into an Erlenmeyer flask (ground-glass stopper) containing 25 ml 2% sulfuric acid and 25 ml water were introduced a weighed amount (about 0.2 g) of the ether and 25 ml 0.2 N bisulfite solution. The contents of the flask were vigorously shaken for 15 minutes and then allowed to stand for 15 minutes. The excess of bisulfite was then titrated with 0.1 N iodine. The calculation was effected according to the formula:

$$\% \text{ acetal} = \frac{(a-b)\cdot M}{\text{weight of sample}\cdot K},$$

Ether investigated	Weight of sample (g)	a	b	% acetal
 $CH_2O-CH(CH_3)-OC_2H_5$ $C\equiv C$ $CH_2O-CH(CH_3)-OC_2H_5$	0.1540	37.40	10.76	99.60
	0.1564	37.40	10.72	98.22
 $CH_2O-CH(CH_3)-OC_2H_5$ $C\equiv C$ CH_2OH	0.2034	37.78	12.34	99.00
	0.1952	37.78	13.49	98.50
 $CH_2O-CH(CH_3)-OC_4H_9$ $C\equiv C$ $CH_2O-CH(CH_3)-OC_4H_9$	0.1210	51.75	34.72	100.70
	0.1245	51.75	34.34	100.10
 $CH_2O-CH(CH_3)-OC_4H_9$ $C\equiv C$ CH_2OH	0.0904	30.61	9.95	102.40
	1.1200	30.61	17.22	103.80

where a is the amount of 0.1 N iodine per ml consumed in titration of 25 ml bisulfite; b is the amount of 0.1 N iodine per ml consumed in titration of the excess of bisulfite in the sample; K = 400 for the diether and 200 for the monoether.

The experimental results are set out in the table.

Hydrogenation of the di-α-butoxyethyl ether of butynediol. 20 g α-butoxyethyl ether of butynediol (b.p. 152-153° at 3 mm) was placed in a "duck" together with 62 g methyl alcohol. The amount of hydrogen taken up after shaking for 2 hours in presence of a catalyst (platinum oxide) was 3.53 l (the theoretical requirement is 3.14 l). After hydrogen had ceased to be taken up (one bubble in 10 minutes), the hydrogenation product was filtered from catalyst, the methyl alcohol was distilled off, and the residue fractionated in vacuum. First fraction 33-37° at 14 mm, 11.8 g; second fraction, 37-120° at 14 mm, 0.2 g; third fraction 120-127° at 14 mm, 3.3 g; residue 0.3 g.

Repeated fractionations of the first fraction yielded butyl alcohol with b.p. 115-116° (756 mm); n_D^{20} 1.3990; d_4^{20} 0.8037.

Three fractionations of the third fraction gave butylene glycol with b.p. 106-107° (3 mm); n_D^{20} 1.4055; d_4^{20} 1.0170; MR_D 23.60; calculated 23.72 [13].

3.325 mg substance: 6.455 mg CO_2; 3.390 mg H_2O. 4.185 mg substance: 8.084 mg CO_2; 4.315 mg H_2O. Found %: C 52.94, 52.71; H 11.41, 11.54. $C_4H_{10}O_2$. Calculated %: C 53.30; H 11.18.

SUMMARY

1. The method of synthesis of butynediol by condensation of acetylene with formaldehyde was improved. The influence of temperature, pressure and catalyst on the course of the reaction was demonstrated and butynediol was obtained in a yield of over 70%.

2. The possibility was established and the conditions found for the synthesis of the mono- and di-α-alkoxyethyl ethers of butynediol.

3. Four α-alkoxyethyl ethers of butynediol, not previously described in the literature, were isolated and characterized: The mono- and di-α-butoxyethyl ethers and the mono- and di-α-ethoxyethyl ethers. Their structure was established by hydrolysis.

4. It was shown that the synthesis of the di-α-alkoxyethyl ethers of butynediol proceeds via the formation of the mono-α-alkoxyethyl ethers whose yield depends on the initial amount of vinyl ether and on the duration of the process.

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REACTIONS OF ALIPHATIC DIAZO COMPOUNDS WITH UNSATURATED COMPOUNDS

XIII. REACTION OF ETHYL DIAZOACETATE WITH ALLYL IODIDE AND WITH NORMAL AND TERTIARY BUTYL BROMIDES IN PRESENCE OF COPPER CATALYSTS

I. A. Dyakonov and N. B. Vinogradova

Following up our investigations in this field [1,2] we have studied the action of ethyl diazoacetate on allyl iodide in presence of copper bronze, using the previously applied procedure. The tendency toward formation of ethyl fumarate during decomposition of ethyl diazoacetate in presence of copper was inhibited by introducing allyl iodide in considerable excess over the quantity required by the equation (1):

$$CH_2{=}CHCH_2I + N_2CHCOOC_2H_5 \xrightarrow{Cu} \underset{(I)}{CH_2{=}CH{-}CH_2CHI{-}COOC_2H_5} + N_2 \qquad (1)$$

It was found that equation (1) represents the main direction of the reaction.

The crude ester (I) was isolated in a yield of 70% of theory and the analytically pure substance in 47% yield. Serious losses arose in purifying the crude preparation, due to the low thermal stability of ester (I) and to contamination with traces of ethyl iodoacetate $ICH_2COOC_2H_5$ (II). The latter could not be isolated but its presence was manifested by the strong lachrymatory effect. Further evidence of its presence was obtained by the results of dehalogenation of the lower boiling fraction of the crude iodine-containing preparation (dehalogenation yielded a mixture of acetic and allylacetic acids, corresponding in composition to the initial mixture of ethyl bromoacetate and ethyl bromoallylacetate).

Ester (I) differed from the esters of α-bromo- [1] and α-chloroallylacetic acids [2], previously prepared by us, also in its behavior toward aqueous alkali solutions. Whereas the chloro- and bromo-esters, as previously shown [1,2] yield predominantly α-hydroxyallylacetic acid when heated with 10% potassium carbonate and only an insignificant amount of vinylacrylic acid, ethyliodoacetate (I) in the same conditions gives mainly vinylacrylic acid (III) or its polymer (equation 2).

Allylhydroxyacetic acid (IV), obtained in negligible yield, was characterized in the form of its anilide:

$$\begin{tikzcd}[column sep=small] (I) \arrow[r, "60\%", "K_2CO_3"'] \arrow[dr, "K_2CO_3\ traces"'] & \underset{(III)}{(CH_2{=}CH{-}CH{=}CH{-}COOH)} \arrow[r] & \underset{polymer}{(C_5H_6O_2)_x} \\ & \underset{(IV)}{CH_2{=}CH{-}CH_2{-}CHOH{-}COOH} \arrow[r, "C_6H_5NH_2"] & \underset{anilide}{C_{10}H_{11}NO_2} \end{tikzcd} \qquad (2)$$

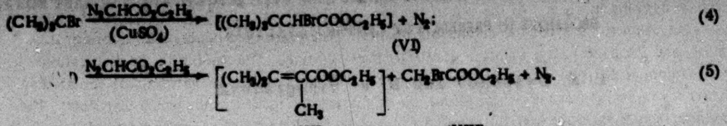
Reduction with hydrogen of ester (I) in an acetic acid medium gave the ester of allylacetic acid (V) which has been described in the literature [7] and which we obtained by the analogous reduction of the ester of α-bromoallylacetic acid [1]. The structure of ester (V) was confirmed by permanganate oxidation which yielded succinic and acetic acids:

$$(I) \xrightarrow[(65\%)]{H_2} \underset{(V)}{CH_2{=}CHCH_2CH_2COOC_2H_5}; \xrightarrow[46\%]{KMnO_4} HOOCCH_2CH_2COOH + CH_3COOH + CO_2. \qquad (3)$$

The transformations of ester (I) represented by equations (2) and (3) not only characterize its properties but also confirm its structure.

Normal and tertiary butyl bromides do not react with ethyl diazoacetate in presence of copper catalysts with formation of the esters of the corresponding α-bromo acids, as would have been expected by analogy with the cases previously investigated by us. With n-butyl bromide the sole reaction product was ethyl fumarate; in the case of tert. butyl bromide, ethyl bromoacetate (VIII) was obtained in addition to ethyl fumarate.

We explain the formation of this substance by cleavage of hydrogen halide from the ester of α-bromoisovaleric acid (VI) formed in the first place and which at once rearranges into the ester of trimethylacrylic acid (VII):

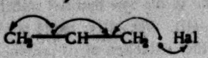


$$(CH_3)_3CBr \xrightarrow[(CuSO_4)]{N_2CHCO_2C_2H_5} \underset{(VI)}{[(CH_3)_3CCHBrCOOC_2H_5]} + N_2; \tag{4}$$

$$\xrightarrow{N_2CHCO_2C_2H_5} \underset{(VII)}{\left[(CH_3)_2C{=}\underset{CH_3}{\underset{|}{C}}COOC_2H_5\right]} + \underset{(VIII)}{CH_2BrCOOC_2H_5} + N_2. \tag{5}$$

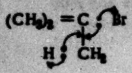
Only ethyl bromoacetate (b.p. 159°) was isolated from the reaction products; it was freed from the conjectured trimethylacrylic acid (b.p. 155°) by treatment with cold potassium permanganate solution. After this treatment the bromine content was still lower than the calculated value; conclusive evidence of the structure was obtained by conversion of a portion of the material into acetic acid by reductive dehalogenation in an alkaline medium.

Taking into account the previous [1,3] ideas about the radical mechanism of heterogeneous catalytic reactions of ethyl diazoacetate, we may suggest that the rupture of the C–Hal bond in allyl halides during attack on the alkylene radical $>CH{-}COOC_2H_5$ will promote the effect of the homolytic conjugation of the $\sigma-\pi$-bonds [4] (A).



(A)

The magnitude of this effect must be inversely proportional to the electronegativity of the halogen atom in the allyl halide, i.e., I > Br > Cl. The experimental data are in satisfactory agreement with this order, judging by the yields of the corresponding α-haloallylacetic esters in the investigated reaction: I- and Br-esters about 70%; the Cl-ester 10.9% of the theoretical yield.*



(B)

In tert.-butyl bromide the homolytic effect of conjugation is also apparently sufficient for development of a similar reaction but on a very much smaller scale than with allyl halides (B).

In n-butyl bromide this effect is not manifested during attack of the alkylene radical.

The mechanism of formation of haloacetic esters demands another explanation. As we know, ethyl diazoacetate (in noncatalyzed reactions) may detach the elements of hydrogen halides from some esters of halo-substituted liquid acids with formation of the corresponding haloacetic esters [5]. We suggest that in the present case also the haloacetic esters are formed by reaction of ethyl diazoacetate, which has failed to come into contact with the copper, with the α-haloallylacetic esters formed according to the proposed catalytic scheme. Since ethyl diazoacetate in itself is not a reagent of the radical type but rather of the nucleophilic type (binding, for example, a proton to the unstable diazonium cation $N_2CH_2COOC_2H_5{}^+$ [6]), then the formation of haloacetic esters must apparently proceed through heterolytic rupture of the C–Hal and C–H bonds in the molecule of the original haloallylacetic ester.

In the case of allyl bromide and iodide the yields of haloacetic esters are very low (about 1% of theory), which may be explicable on the basis of more successful competition in these cases of the homolytic reaction with participation of the free alkylene radical $>CHCOOC_2H_5$. In the case of allyl chloride and tert.butyl bromide the main (radical) reaction proceeds less energetically, and consequently higher yields of haloacetic esters are obtained: $ClCH_2COOC_2H_5$ – 9.8% and $BrCH_2COOC_2H_5$ – 9.1% of the theoretical yield.

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* Calculated on the crude preparation.

EXPERIMENTAL

I. Condensation of ethyl diazoacetate with allyl iodide. 560 g dry, freshly distilled allyl iodide and 0.8 g copper bronze ("Natur Cupfer C") are introduced into a three-necked round-bottomed flask fitted with mechanical stirrer, dropping funnel and reflux condenser. The allyl iodide is heated to the boil, the stirrer is started up, and a solution of 175 g ethyl diazoacetate in 175 g allyl iodide is run in from the dropping funnel. The nitrogen evolved during the reaction is collected in a gasholder after passing in succession through a reflux condenser and a trap immersed in freezing mixture. At the end of the reaction 29.5 l nitrogen (18°, 767 mm) had been evolved, which was equivalent to 79.3% of the theoretical amount. The reaction product, after cooling, is filtered from catalyst, and the excess allyl iodide is distilled off at 100 mm. The residue in the distillation flask (a dark-colored liquid) is distilled in a 4 mm vacuum. Partial decomposition of the material occurred during the distillation with cleavage of molecular iodine which imparted a reddish color to the distillate. The yield of crude ethyliodoallyl acetate (I) with b.p. 65-82° at 4 mm was 274.3 g (70% of the theoretical).

Vacuum fractionation of crude ester (I)

No. of fraction	Boiling range	n_D^{20}	Weight (g)
1	77-90° at 12 mm	1.4945	6.3
2	49-56° at 1 "	1.4950	10.4
3	56-65° at 1 "	1.5005	9.5
4	65-66° at 1 "	1.5062	183.7

The undistillable residue weighed 60 g (resinified products). The crude reaction product was repeatedly fractionated in vacuum for isolation of the pure ester (I). The molecular iodine released during the distillations was removed from the distillate by shaking with mercury.

Fraction 4 is the analytically pure preparation of ester (I) (yield 47% of theory). Fractions 1-3 were assumed to be a mixture of the esters of iodoacetic and iodoallylacetic acids. The first of these was subjected to reductive dehalogenation for the purpose of obtaining acetic acid and so demonstrating the presence of iodoacetic acid in this fraction.

5.7 g of the material of Fraction 1, 10 ml water and 45 g 30% sodium amalgam were shaken for 3 hours under external cooling. After the mercury had been separated, the solution was boiled for 4 hours with 200 ml 5% potassium hydroxide solution. The cooled alkaline solution was acidified with tartaric acid (30 g) and the volatile acids distilled off with steam.

Fractional precipitation with $AgNO_3$ solution of the neutralized alkaline distillate gave three fractions of silver salts which were analyzed for their silver content.

Found %: Ag I 54.82, 55.13; II 58.12, 58.42; III 60.29. $C_5H_7O_2Ag$. Calculated %: Ag 52.13. $C_2H_3O_2Ag$. Calculated %: Ag 64.66.

II. Ethyl α-iodoallylacetate. A colorless oil with a pleasant ethereal odor; b.p. 62-66° at 1 mm.

d_4^{20} 1.558; n_D^{20} 1.5062; MR_D 48.45; calculated 48.51. 0.2248 g, 0.3641 g substance: 0.2088 g, 0.3385 g AgI. 0.3799 g, 0.1618 g substance; 21.21, 20.58 g C_6H_6; Δt 0.39°, 0.16°. Found %: I 50.23, 50.25; M 235.6, 251.7. $C_7H_{11}O_2I$. Calculated %: I 49.97; M 254.0.

Dehalogenation. To a mixture of 60 g ester (I), 60 ml alcohol and 90 g 65% acetic acid, heated on a water bath to 65°, was added 20 g zinc dust in small portions. The mixture was then refluxed for one hour, the unreacted zinc dust was filtered off after cooling, the solution neutralized with soda, and the ester was extracted with ether.

The ethereal solution was dried with sodium sulfate; the ether driven off and the residual ethyl allyl acetate distilled in vacuum. The yield of ester with b.p. 43-44° at 12 mm [7] was 19.7 g (65.2% of the theoretical yield).

d_4^{20} 0.9016; n_D^{20} 1.416; MR_D 35.67; calculated 35.71.

0.2180 g substance: 0.5225 g CO_2; 0.1859 g H_2O. Found %: C 65.36; H 9.53. $C_7H_{12}O_2$. Calculated %: C 65.58; H 9.45.

Oxidation of the ester with potassium permanganate. 10 g of the ester was treated in the cold with 3% $KMnO_4$ solution. 20.9 g of permanganate was consumed. After the usual treatment the nonvolatile and the steam-volatile acids were separated by the usual method. The steam-volatile acids were examined in the form of their silver salts.

0.0934 g substance: 0.0605 g Ag. Found %: Ag 64.79. $C_2H_3O_2Ag$. Calculated %: Ag 64.66.

Succinic acid was found in the solution of the acids non-volatile in steam. Yield 46% of the theoretical. M.p. 182°. It did not depress the melting point of an authentic sample of succinic acid.

0.1665 g substance: 27.93 ml 0.1 N NaOH. Found: equiv. 59.61. $C_4H_6O_2$. Calculated: equiv. 59.0.

Hydrolysis of ester (I). 50 g of ester (I) was hydrolyzed by heating with 10% potassium carbonate solution under good stirring. The resultant solution was concentrated to a volume of 150 ml, acidified with sulfuric acid until acid to Congo, and extracted with ether in a Soxhlet. The ethereal extract yielded 16.5 g viscous, yellow oil which partially crystallized when cooled with a freezing mixture. On attempted filtration the crystals deliquesced on the filter. It was only possible to isolate an insignificant amount of colorless, prismatic crystals which after standing for 12 hours in a vacuum desiccator were converted into a resinous mass of polymer. We assumed that the latter was a polymer of vinylacrylic acid and that the crystals were the monomer. The polymer dissolved when heated in alkalies and again came down when acidified*.

0.1850 g substance: 36.4 ml 0.1 N NaOH. Consumed 18.7 ml 0.1 N HCl. Found: equiv. 104.6 $(C_4H_5COOH)_x$. Calculated: equiv. 98.1.

The residual oil polymerized almost completely after standing for five days, giving 10 g polymer. The unpolymerizable portion of the oily acid was extracted with ether. The very small quantity of liquid acid obtained after evaporation of the ether was characterized by conversion into the anilide by the method developed for the preparation of anilides of monocarboxylic acids and their sodium salts [9]. The unrecrystallized anilide melted at 74-75°. Its mixture with the anilide of authentic α-hydroxyallylacetic acid (m.p. 77-78° [2]) melted at 75-76°. The investigated acid was therefore assumed to be hydroxyallylacetic acid.

III. Action of ethyl diazoacetate on tert. butyl bromide in presence of copper sulfate. Using the procedure and apparatus described in part I above, 360 g freshly distilled tert. butyl bromide, 0.5 g anhydrous copper sulfate and 135.7 g ethyl diazoacetate were brought into reaction.

After distilling off the excess butyl bromide, the reaction product was distilled in a 5 mm vacuum. A considerable amount of resinous material remained in the distilling flask and two liquid fractions were obtained: I with b.p. 35-55° at 5 mm (20.9 g) and II with b.p 55-80° at 5 mm (38.7 g).

Examination of fraction I. It was intensely lachrymatory and contained halogen. Fractionation in a column at normal pressure yielded 15.1 g substance with b. p. 156-160°.

n_D^{20} 1.4455; d_4^{20} 1.414.

0.1467 g substance, 0.1241 g AgBr. Found %: Br 35.99. $C_4H_7O_2Br$. Calculated %: Br 47.84.

The constants of ethyl bromoacetate reported in the literature [10] are: b. p. 159°; d_4^{13} 1.51414; n_D^{13} 1.45420.

Unsaturated impurities in the investigated fraction were removed by shaking in the cold with 3% permanganate solution (the permanganate consumption was 1 g for 14.5 g substance). After vacuum distillation the substance had b p. 156-160°; n_D^{15} 1.4485.

0.3030 g, 0.2985 g substance: 0.0989 g, 0.0985 g AgBr. 0.1666 g, 0.3376 g substance; 15.05, 15.05 g C_6H_6: Δt 0.37°, 0.74°. Found %: Br 41.93, 42.38; M 153.5, 155.5. $C_4H_7O_2Br$. Calculated %: Br 47.84, M 167.0.

The material of fraction I was dehalogenated in the above manner. Only acetic acid was detected in the dehalogenation product after hydrolysis. It was identified through the silver salt:

0.1102, 0.1371 g salt: 0.0713, 0.0879 g Ag. Found %: Ag 64.71, 64.12. $C_2H_3O_2Ag$. Calculated %: Ag 64.66.

Examination of fraction II. Fractionation gave 20.2 g liquid with the characteristic odor of ethyl fumarate and boiling at 65° at 1.5 mm; d_4^{20} 1.0593; n_D^{20} 1.4410. The literature [11] gives b. p. 96° at 10 mm; n_D^{20} 1.4410; d_{20}^{20} 1.0535. The identity was confirmed by saponification with potassium hydroxide in methyl alcohol to form a precipitate of potassium fumarate; from the latter, diphenacyl fumarate was prepared with m. p. 197° (the literature [12] reports 197°). It did not depress the melting point of a sample of authentic diphenacyl ester.

IV. Action of ethyl diazoacetate on n-butyl bromide in presence of copper bronze. Condensation of 68 ml n-butyl bromide with 11.4 g ethyl diazoacetate was performed by the usual procedure (see section I above) in presence of 0.5 g copper bronze. The catalyst was then filtered off and the unreacted butyl bromide (63 ml) was distilled off at 142 mm. The weight of the residue in the distilling flask was 10.2 g. Fractionation of this residue at 9 mm gave 3.2 g liquid with the odor of ethyl fumarate and b. p. 91-92°; n_{α}^{20} 1.437 (yield 37.2%). The weight of unreacted residue was 6.9 g.

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* According to the literature [8] the monomer of vinylacrylic acid forms colorless, very hygroscopic prisms with m.p. 80°. Readily soluble in alcohol and water. On standing it polymerizes to a solid polymer.

Literature constants for ethyl fumarate [11]: b. p. (10 mm) 96°; n_{α}^{20} 1.437625.

SUMMARY

1. It is shown that reaction of ethyl diazoacetate with allyl iodide in presence of copper powder gives about a 70% yield of α-iodoallylacetic ester together with an insignificant amount of ethyl iodoacetate.

2. Some reactions of ethyl α-iodoallyl acetate were studied and the results were compared with those of similar experiments with chloro- and bromoallyl acetic esters.

3. Condensation of ethyl diazoacetate with tert.- and n-butyl bromides led to isolation in the first case of the esters of fumaric and bromoacetic acids and in the second case of only the ester of fumaric acid. It is suggested that the ester of α-bromoisovaleric acid is formed as an intermediate product in the reaction with tert.-butyl bromide.

4. A reaction mechanism is proposed for the formation of haloallylacetic and haloacetic esters in the reaction of ethyl diazoacetate with alkyl halides in presence of copper catalysts.

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THE STRUCTURE OF OLEIC ACID

A. K. Plisov and E. G. Maleeva

The structure of the geometrically isomeric monobasic acids has not yet been definitely established, and even such familiar acids as oleic and elaidic are sometimes regarded as cis-isomers and sometimes as trans-isomers [1].

The problem of the determination of the cis- and trans-isomers of aliphatic and cyclic compounds is an extremely difficult one. When the molecule of the substance contains two radicals capable of acting on each other, the formation of an intramolecular derivative (anhydride, lactam, etc.) is characteristic of cis-isomerism. Apart from such clearly definable cases, up to recent times no other criteria were available except the definition of a trans-isomer as a substance which is more stable, has a higher melting point and is chemically less active. These criteria spring from analogy with certain cases which are known to be unrelated to the present cases. Nevertheless it is already clear than even these methods are not universally applicable. Thus, some trans-forms are known whose melting points are lower than those of the isomeric cis-forms. We could cite a long list of fundamental attempts to find a valid method for determining the actual structure of cis- and trans-isomeric compounds. This clearly demonstrates how difficult is the problem and how few solutions have been obtained.

One of the present authors once suggested that on the basis of the theory of steric hindrance we should expect different reactivities on the part of geometrical isomers and their derivatives. In that event a chemical solution should be possible of the problem of the true configuration of unsaturated compounds with cis-trans isomerism (a hitherto unsolved problem) if we consider those derivatives of acid which do not contain groups readily capable of reacting intramolecularly with one another.

Considering the case of oleic acid and its derivatives such as esters, we may assume on the basis of the theory of steric hindrance that all reactions associated with the double bond of the cis-form, such as addition of hydrogen, halogens, hydrogen halides and oxygen must proceed more readily than in the case of the trans-form, in which the action on the double bond of molecules of reactants will be hindered by the $CH_3(CH_2)_7$ and $(CH_2)_7COOH$ radicals which block the space near the double bond from two sides. This crowding does not occur to the same extent in the cis-form where both radicals are attached at one side of the double bond. Concerning reactions involving the carboxyl group of oleic acid or its esters, the reaction of a molecule of an alcohol with the carboxyl group or that of alkali with the ester group will proceed more readily in the trans-form and will be hindered in the cis-form, because the space in the vicinity of the carboxyl or ester group in the cis-form is occupied by the radical $CH_3(CH_2)_7$, and molecules of alcohol or alkali must first overcome the hindrance created by the hydrocarbon radical. This difficulty will not arise with the trans-form. Consequently the esterification of oleic acid and the saponification of its esters should proceed with greater difficulty in the case of the cis-form than in the case of the trans-form. Esterification or saponification of the esters may possibly proceed in the cis-form the more slowly the more branched is the alcohol radical. We must assume that the entry of a radical into the molecule introduces something more than just congestion of the space: it introduces what we may call the chemical effect of the radical. The chemical effect can vary substantially with the reactions, some of which are hindered while others are facilitated. Concerning the steric effect, it comes into play – if not always with equal intensity then at any rate in some degree – for all reactions which take place directly at the group in question; The resultant of both effects is the same and is accessible to experiment. In some cases this resultant may have a reverse effect in relation to the steric effect. When a compound contains radicals with a weakly manifested chemical individuality, e.g., alkyls, the chemical effect will be weak and hardly capable of opposing steric hindrance. Applying the theory of steric hindrance to cis- and trans-forms, in the case under consideration we can expect definite assistance from it: the chemical effect of the radical will be sufficiently similar in both isomers, but the steric effect will be considerably different.

We have studied the reactions of oxidation and hydrogenation [2] of oleic and elaidic acids and the saponification, hydrogenation and oxidation of methyl oleate and methyl elaidate. The velocities of these reactions were found to differ in methyl oleate and methyl elaidate. Methyl oleate is saponified more slowly than elaidate but is oxidized and hydrogenated more rapidly than elaidate.

The results make it appear that a cis- and trans-structure must be, respectively, ascribed to oleic acid (and methyl oleate) and elaidic acid (and methyl elaidate).

EXPERIMENTAL

The methyl esters of oleic and elaidic acids were prepared from the pure silver salts of the acids and methyl iodide and had the following constants:

Methyl oleate: b. p. 213−213.5° at 15mm; d_4^{16} 0.8780;

K_0 189 (calculated K_0 189.1) K_p0.

Methyl elaidate: b. p. 214° 15 mm; d_4^{16} 0.8790; K_0 189; K_p0.

1. Determination of relative velocities of saponification of methyl oleate and methyl elaidate. Each ester was weighed out in quantity of 0.1480 g (1/2000M) into a small glass cylinder with a ground-glass stopper into which were sealed two platinum electrodes. Addition was made of 5 ml 96% alcohol and 5 ml 0.1 N alcoholic KOH and a first determination of electric conductivity was made with the help of a resistance bridge and a lamp-type optical indicator. Each experiment was assumed to start from the instant of addition of the alcoholic potash to the ester; then at definite intervals of time the electric conductivity of the alcohol solution was measured at a temperature of 25°, the conductivity being a direct measure of the hydroxyl ion concentration. The significant feature in this connection is the fall in conductivity, i.e., the fall in conductivity during a specified interval of time. In the present case the fall of electric conductivity depends on the reaction between alkali and ester (during which the hydroxyl ions which are responsible for the good conductivity of the solution gradually disappear and are replaced by the salts of oleic or elaidic acid which are characterized by poor conductivity). The ester and glycerol do not exert an important influence on the electric conductivity so that the fall in electric conductivity is a measure of the progress of the saponification reaction.

In Table 1 are set out the results of measurement of the electric conductivity of the reaction medium during saponification of the methyl esters of oleic and elaidic acids.

TABLE 1

No.	Duration of experiment (minutes)	Electric conductivity·10^4	Fall of electric conductivity	Maximum change in electric conductivity as % of the initial conductivity
		Saponification of methyl oleate		
1	0	555	−	12
	30	512	43	
	90	488	67	
	150	486	69	
2	0	500	−	12
	30	454	46	
	90	434	66	
	150	430	70	
		Saponification of methyl elaidate		
3	0	500	−	17
	30	454	46	
	90	434	66	
	150	412	88	
4	0	555	−	16
	30	500	55	
	90	474	81	
	150	465	90	

Similar results were obtained in saponification experiments carried out at a temperature of 28°.

2. Hydrogenation of methyl esters of oleic and elaidic acids. Hydrogenation was effected in presence of platinum deposited on $BaSO_4$; materials used in each experiment were 0.25 g $BaSO_4$ and 0.008 g metallic platinum, 15 methyl alcohol and 0.8 g methyl oleate or elaidate. Experiments were run simultaneously with the two esters at 25° in a hydrogenation "goose." Blank experiments with pure oleic and elaidic acids were run in order to establish the degree of activity of the catalyst and for the purpose of comparison. Hydrogenation results are in Table 2.

Oxidation of oleic and elaidic acids and of their methyl esters. Oxidation was studied by the reaction with potassium permanganate when, as we know, both acids react to form the dihydroxystearic acids. We found that oleic and elaidic acids react with potassium permanganate at different speeds. The course of the oxidation could be followed by the change in electric conductivity of the $KMnO_4$ solution, the conductivity rising appreciably with progressive consumption of the oxidizing agent, since the place of the decomposed $KMnO_4$ was taken by molecules of KOH which are known to possess a higher conductivity.

TABLE 2

Duration of hydrogenation in minutes from start of expt.	ml H_2 absorbed (a)			
	oleic acid	elaidic acid	methyl oleate	methyl elaidate
20	48	37	46	35
40	81	72	80	70
60	104	90	103	90

$$\frac{{}^{a}\text{oleate}}{{}^{a}\text{elaidate}} = \frac{103}{90} = 1.14:1;$$

$$\frac{{}^{a}\text{oleic acid}}{{}^{a}\text{elaidic acid}} = \frac{104}{90} = 1.15:1.$$

In the present case, therefore, the rising electric conductivity of the $KMnO_4$ solution in contact with the oleic or elaidic acid or their esters served as a criterion of the decomposition velocity of $KMnO_4$ and in turn of the velocity of the oxidation reaction. Concerning the formation during this reaction of the salt of the organic acid at the expense of the alkali formed during deoxidation of the $KMnO_4$, this process here proceeds so slowly that it has no substantial effect on the measurement of the electric conductivity of the solution.

The oxidation experiments were performed simultaneously with identical weights of the acids and esters (1 / 5000 mole) introduced as in the saponification experiments in identical vessels fitted with platinum electrodes. To each of the samples was added 5 ml 1.5% aqueous $KMnO_4$ solution and the first determination of electric conductivity was quickly made. Before the mixing, each reagent had been kept in a thermostat for 15 minutes. Oxidations of the acids were performed at 48° and those of the esters at 25°. Table 3.

TABLE 3

Number of experiment	Duration (minutes)	Electric conductivity $\cdot 10^4$	Increase in electric conductivity	Maximum change in electric conductivity in % of initial conductivity
		Oxidation of oleic acid		
1	0	514	–	38.9
	15	666	152	
	30	714	200	
	45	714	200	
		Oxidation of elaidic acid		
2	0	514	–	26.2
	15	598	84	
	30	647	133	
	45	649	135	
		Oxidation of methyl oleate		
3	0	430	–	19
	30	446	16	
	60	472	42	
	120	488	50	
	180	511	81	
		Oxidation of methyl elaidate		
4	0	434	–	12.4
	30	444	10	
	60	454	20	
	120	476	42	
	180	488	54	

SUMMARY

1. It is establish that oleic and elaidic acids and their methyl esters exhibit different reactivities.

2. Methyl elaidate is saponified more rapidly than methyl oleate.

3. Elaidic acid and its methyl ester are hydrogenated and oxidized with greater difficulty than oleic acid and its methyl ester.

4. The reactivity of oleic and elaidic acids and their methyl esters is consistent with the theory of steric hindrance and confirms their structure as, respectively, cis- and trans-isomers.

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DIRECT SYNTHESIS OF ALKYL- AND ARYLHALOSILANES

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The preparation of alkyl- and arylhalosilanes by the action of haloalkyl(aryl) derivatives on silicon in presence of a catalyst was first described in 1945 [1]. This reaction gives a mixture of halogen-containing organosilicon compounds with various ratios of halogen to organic radical, namely, $RSiX_3$; R_2SiX_2; R_3SiX; SiX_4; SiR_4, etc. R is an organic radical and X is halogen.

These compounds are formed according to the following schemes:

1. $2RX + Si \rightarrow R_2SiX_2$;
2. $3RX + Si \rightarrow R_3SiX + X_2$;
3. $3RX + Si \rightarrow RSiX_3 + 2R$;
4. $2X_2 + Si \rightarrow SiX_4$;
5. $4RX + 2\ Si \rightarrow SiR_4 + SiX_4$

Depending on the conditions the main product will be various halo-substituted alkyl- and arylsilanes, especially R_2SiX_2.

The lowest temperature at which this reaction commences is the optimum for the addition of an organic radical to silicon; with rising temperature the reaction velocity increases but at the same time the final mixture of products becomes richer in halogen, until $SiCl_4$ is reached, and correspondingly poorer in carbon and hydrogen. The reaction velocity also depends on the nature of the organic radical, of the halogen and of the catalyst.

Of great importance for obtaining good yields of alkyl- and arylhalosilanes is the quality of the catalyst. Copper is an active catalyst in the reaction of silicon with alkyl and aryl halides. It accelerates the reaction and permits operation at a lower temperature, although the role of copper in the mechanism of this reaction is still not altogether clear.

A direct synthesis has been utilized industrially for the production of methylchlorosilanes and phenylchlorosilanes [2]. In our research we set ourselves the task of studying the direct synthesis of methylbromosilanes and phenylbromosilanes [3,4].

The work was carried out in the department of organic and petroleum chemistry of the Acad. I. M. Gubkin M.N.I.* in 1946-1947 (synthesis of methylbromosilanes) and in 1949 (synthesis of phenylbromosilanes). During the completion of this research a short publication appeared [5] which gave a brief description of the preparation of methylbromosilanes and of their analysis.

EXPERIMENTAL

Methyl bromide was reacted with silicon, also bromobenzene with silicon, in an apparatus consisting of a tube furnace (electrically heated) 0.8 meter long and 40 mm in internal diameter. Two molybdenum glass tubes 1.2 meters long and 15 mm in diameter were inserted in this furnace. Each tube was charged with an intimate mixture of 60 g (80%) silicon and 15 g (20%) reduced copper. The silicon was previously ground to a fine powder in a porcelain mortar. The copper was reduced from copper oxide powder at 300°. The air was displaced from the system with carbon dioxide prior to starting the passage of methyl bromide (for preparation of methylbromosilanes) and of bromobenzene (for preparation of phenylbromosilanes).

Preparation of methylbromosilanes. Preliminary experiments showed that at 250-300° the reaction of methyl bromide with silicon in presence of copper was not sufficiently energetic; systematic experiments were therefore run at temperatures of 320-360°. Table 1 gives the yields of methylbromosilanes at various temperatures.

We see from the table that the best yields are obtained at 330-340°, although deviations of 10° to either side of this range did not cause large changes in yields.

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The rate of passage of methyl bromide is an important factor; if it is too high a large proportion of the methyl bromide fails to react in the tubes and is absorbed in the receivers, which reduces sharply the yields of crude reaction product and leads to heavy losses during fractionation, mainly due to the volatility of the methyl bromide (see experiments 2 and 3, Table 1).

TABLE 1

Formation of Methylbromosilanes at Various Temperatures

No.	Methyl bromide consumed (g)	Temperature of experimental series (°C)	Duration of experiment (hours)	Weight of reaction product		Losses (%)
				before fractionation (in g)	after fractionation of the organosilicon compounds (in g)	
1	1250	320-330	48	648.6	507.3	21.9
2	1250	330-340	57	654	569	11.5
3	1250	330-340	42	823.6	618	25.4
4	1120	350-360	48	620	486	21.5

In otherwise equal conditions the velocity of the reaction appreciably increases on the second day of an experiment, i.e., about 10-12 hours after the start of the series of experiments; this is probably associated with the fact that the reaction mass (silicon + copper) has by that time become more porous, in consequence of which the surface of the reaction zone is increased. On the third day, however, the total yield of reaction product falls appreciably and continues to fall up to the end of the given series of experiments due to gradual consumption of the silicon.

The data of Table 2 illustrate the progress of the reaction in four series of experiments at temperatures of 310-320°, 320-330°, 330-340° and 350-360°.

TABLE 2

Course of Formation of Methylbromosilanes at Various Temperatures

	310-320°			320-330°			330-340°			350-360°		
No.	Duration of experiments (hours)	consumption of methyl bromide (g)	wt. of product (g)	duration of experiments (hours)	consumption of methyl bromide (g)	wt. of product (g)	duration of experiments (hours)	consumption of methyl bromide (g)	wt. of product (g)	duration of experiments (hours)	consumption of methyl bromide (g)	wt. of product (g)
1	12	280	152.4	12	280	119.5	11	250	190	12	280	149.5
2	12	280	166.5	12	280	182.6	9	250	247.3	12.5	280	246.9
3	12	280	90	12	280	108.3	7	250	168.7	12	280	137.6
4	12	280	71.7	12	280	114.4	7.5	250	140.6	12	280	86.7
5	12	280	63	12	280	74.3	7.5	250	77	–	–	–
Total	60	1400	543.6	60	1400	599.1	42	1250	823.6	48.5	1120	620.7

Composition of the products of reaction of methyl bromide with silicon. In order to establish the composition of the gaseous products which volatilized during fractionation, we distilled the mixture of methylbromosilanes, without changing the receivers, to 140°, i.e., to the temperature usually reached in our fractional distillations. The receiver was a Wurtz flask whose exit tube was connected to traps which collected the gaseous products. A water scrubber was the first trap and was separated from the receiver by a calcium chloride tube; the connecting tube of this scrubber was above the surface of the water in order to avoid sucking back. This scrubber was intended for absorption of the hydrogen bromide which our observations showed to be evolved during fractionation. The scrubber was followed by two absorbers which were cooled to −20° with ice-salt mixture. These were intended for condensation of any methyl bromide (b. p. +4°) which did not enter into reaction and which dissolved in large quantity in the mixture of methylbromosilanes.

After several such fractionations of the reaction product we were satisfied that the main portion of the volatile products consisted of methyl bromide. Its quantity was found to depend on the reaction temperature and the rate of flow of the methyl bromide through the reaction zone: the lower the reaction temperature (for a given rate of flow) the greater the amount of methyl bromide in the reaction product. For example, in one experiment performed at 300-310°, after fractionation there was obtained methyl bromide in amounts equivalent to 17% of the product taken for fractionation. In another experiment at 350-360° and the same flow velocity the amount of methyl bromide recovered unchanged was only about 7% of the weight of reaction product fractionated.

It was also established that hydrogen bromide came over and was collected in the water scrubber. After fractionation this scrubber increased considerably in weight. Titration showed that the mean amount of hydrogen bromide was about one percent of the product which was fractionated. About 3% of the volatiles (calculated on the weight of fractioned product) was lost. These may have been the simplest, very volatile substituted silanes formed as by-products of the reaction.

With the aim of isolating the individual methylbromosilanes in the purest possible form we subjected the mixture of crude products to repeated fractionation. All attention was concentrated on the isolation of fractions corresponding to trimethylbromosilane, dimethylbromosilane and methyltribromosilane.

Trimethylbromosilane $(CH_3)_3SiBr$ (b. p. 80°, bromine content 52.21%). Our attempts to obtain this most volatile methylbromosilane have so far given negative results. The fraction with a five-degree boiling range (77-82°) in which we expected to find trimethylbromosilane was analyzed for bromine (Volhard method) and found to contain a higher proportion of bromine (56% or more), apparently due to impurities with a higher bromine content, such as dimethyldibromosilane, etc. In view of the fact that this fraction was extremely small it was impossible to examine it more closely.

We determined the bromine content of the methylbromosilanes by Volhard's method, modified to suit the special case, i.e., after hydrolysis of the bromo compound.

Dimethyldibromosilane $(CH_3)_2SiBr_2$ is the main product of reaction of methyl bromide with silicon. We isolated it in the pure state.

B. p. 112-112.5° (760 mm.) Literature data: b. p. 112.3°. 0.6338 g substance: 4.65 ml 0.1 N $AgNO_3$. 0.7282 g substance: 5.35 ml 0.1N $AgNO_3$. 0.7430 g substance: 5.45 ml 0.1N $AgNO_3$. Found %: Br 73.29, 73.29, 73.28. $C_2H_6SiBr_2$. Calculated %: Br 73.33

Methyltribromosilane CH_3SiBr_3 was isolated in the pure state.

B. p. 133-133.5° at 755 mm; literature data: b. p. 133.5° at 764 mm. 0.9322 g substance: 7.9 ml 0.1N $AgNO_3$. 0.5440 g substance: 4.6 ml 0.2N $AgNO_3$ Found %: Br 84.66, 84.48. CH_3SiBr_3. Calculated %: Br 73.33.

Higher fractions (boiling above 140°). Whereas all the above-described methylbromosilanes were colorless after distillation, the residue following their separation had a dark color (ranging from dark-brown to nearly black). The Volhard determination of bromine (mean of several analyses) in the residue gave a value of 63.5%. On attempting to fractionate this residue we succeeded in isolating a small number of fractions with the boiling point of silicon tetrabromide (151°), after which the temperature rapidly rose to above 200° due to the presence of some more complex products of condensation or polymerization.

General properties of the methylbromosilanes. All the methylbromosilanes are heavy liquids. They fume in the air and are hygroscopic. They etch glass and carbonize cork. A conspicuous feature is the regular change in boiling point with increasing bromine content (Table 3).

TABLE 3

Boiling Points of Methylbromosilanes

	$(CH_3)_3SiBr$	$(CH_3)_2SiBr_2$	CH_3SiBr_3	$SiBr_4$
Boiling point	79.9°	112.3°	133.5°	151°

TABLE 4

Boiling points of Methylchlorosilanes

	$(CH_3)_3SiCl$	$(CH_3)_2SiCl_2$	CH_3SiCl_3	$SiCl_4$
Boiling point	57.6°	70°	66°	59°

This regularity contrasts with the variation of boiling points of the methylchlorosilanes shown in Table 4: with increasing chlorine content the boiling point at first rises and then (starting from methyltrichlorosilane) begins to fall, so that the boiling point of tetrachlorosilane is only 1.4° higher than that of trimethylchlorosilane.

Preparation of the phenylbromosilanes*. Preliminary experiments on the preparation of the phenylbromosilanes showed that the reaction of bromobenzene with silicon was not sufficiently energetic at temperatures below 400°. The yield of organosilicon compounds was about 20%. Systematic experiments with the aim of establishing the optimum reaction temperature were therefore carried out at temperatures of 400-500° (Table 5).

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* N.M. Zhmykhova participated in the synthesis of the phenylbromosilanes.

TABLE 5

Preparation of Phenylbromosilanes at Various Temperatures

No. of preparation	C_6H_5Br passed through (in g)	Temp.	Duration of expt. (hours)	Wt. of reaction products (g)	Amount of organosilicon compounds	
					(in g)	(in %)
1	700	400-410°	70	686	324.8	47.4
2	700	410-420	56	662.1	374.6	56.5
3	700	420-430	51	659.4	336.9	51
4	700	440-460	56	684.5	348.1	50.8
5	700	480-500	91	532.6	258	48.4

TABLE 6

Effect of Flow Rate of Bromobenzene on the Reaction Yield at 420-430°

No. of preparation	C_6H_5Br passed through (g)	Duration of experiments (hours)	Weight of reaction products (g)	Amount of organosilicon compounds	
				(in g)	(in %)
1	276	20	260.0	131.3	50.5
2	450	24	434.0	184.0	42.5

TABLE 7

Course of Formation of Phenylbromosilanes with Passage of Time at Various Temperatures

No. of preparation	410-420°			440-460°		
	Duration of experiments (hours)	Consumption of bromobenzene (g)	Amount of organosilicon compounds formed (g)	Duration of experiments (hours)	Consumption of bromobenzene (g)	Amount of organosilicon compounds formed (g)
1	6	75	31	6	75	30.4
2	6	75	53	6	75	69
3	6	75	45.7	6	75	54
4	6	75	44	6	75	40
5	6	75	38	6	75	37
6	6	75	30	6	75	30
7	6	75	25	6	75	28
Total..	42	525	266.7	42	525	288.4

The table shows that the best yields of phenylbromosilanes are obtained at temperatures of 410-420°.

The speed of flow of the bromobenzene during the reaction is very important. If the speed is too low, much of the bromobenzene fails to react and the yields of phenylbromosilanes are low.

Table 6 illustrates the effect of flow velocity of the bromobenzene on the yield of phenylbromosilanes.

In the preparation of phenylbromosilanes, just as in that of methylbromosilanes, the reaction velocity increases in the first 10-12 hours after the start of a given series of experiments and then gradually decreases due to consumption of the silicon (Table 7).

Composition of Products of Reaction of Bromobenzene with Silicon in Presence of a Catalyst (Copper)

The composition of the products was investigated by subjecting the mixture to fractionation.

Table 8 gives details of the fractionation of mixtures of phenylbromosilanes prepared by direct synthesis at various temperatures.

We established that the obtained wide-range fractions are technical products with essentially the following compositions: First fraction — unreacted bromobenzene and silicon tetrabromide; second fraction — phenyltribromosilane, not previously described in the literature; third fraction — intermediate; fourth fraction — diphenyldibromosilane; the residue at above 200° at 12 mm contained a small amount of triphenylbromosilane.

For the purpose of isolation of the individual phenylbromosilanes the prepared fractions (Table 8) were cut at 12 mm into narrower fractions which were then tested for constancy of composition. We determined the bromine content of the phenylbromosilanes by two methods which checked each other: Alkali saponification and the Volhard method.

Table 9 gives the yields of silicon tetrabromide and of phenylbromosilanes at various experimental temperatures.

We see from Table 9 that with rising temperature the yields of phenyltribromosilane and silicon tetrabromide increase but the yield of diphenyldibromosilane decreases.

TABLE 8

Fractionation of Mixtures of Phenylbromosilanes Prepared by Direct Synthesis at Various Temperatures (Yield of Fractions Expressed as % of Material Charged)

No. of preparation	Fractions obtained	Experimental temperatures				
		400-410°	410-420°	420-430°	440-460°	480-500°
1	Up to 160° (760 mm)	59.47	50.7	54.7	57.2	56.57
2	110-150° (12 mm)	13.4	24.0	23.6	22.0	22.8
3	150-175° (12 mm)	6.86	2.62	6.15	2.7	6.3
4	175-200° (12 mm)	13.3	15.5	8.3	7.85	5.15
5	Residue above 200°	4.87	6.94	4.23	9.05	5.7
	Losses	2.1	0.24	3.02	1.2	3.48

TABLE 9

Yields of Phenylbromosilanes and Silicon Tetrabromide at Various Experimental Temperatures

No. of preparation	Experimental temperatures	$SiBr_4$	$C_6H_5SiBr_3$	Intermediate fraction	$(C_6H_5)_2SiBr_2$	Residue
1	400-410°	14.4	32.8	14.5	28.0	10.3
2	410-420	13.5	42.4	4.5	27.4	12.2
3	420-430	16.2	46.8	12.2	16.4	8.4
4	440-460	17.1	44.0	5.4	15.6	17.9
5	480-500	17.4	47.2	13.0	10.6	11.8

We were unable to isolate silicon tetrabromide ($SiBr_4$) in the pure state due to the closeness of its boiling point (154°) to that of bromobenzene (157°).

The amount of silicon tetrabromide obtained was determined by hydrolyzing the fraction which came over up to 160°; the bromobenzene was then removed by steam-distillation. At experimental temperatures of 400-500° we obtained 14-17% silicon tetrabromide (Table 9).

Phenyltribromosilane $C_6H_5SiBr_3$. This compound has not previously been described in the literature. Its isolation in the pure form was effected by subjecting the 110-150° (12 mm) fraction to repeated vacuum fractionation into narrower cuts, each of which was analyzed for the bromine content. The fraction with b p. 130-131° at 12 mm had a bromine content closest to that of phenyltribromosilane.

The bromine was determined by saponification with alkali. 0.3779 g substance: 19.6 ml 0.5 N KOH; 13.21 ml 0.5 N H_2SO_4 0.4323 g substance: 19.6 ml 0.5 N KOH; 12.24 ml 0.5 N H_2SO_4. Found %: Br 68.27, 68.80. $C_6H_5SiBr_3$. Calculated %: Br 69.56.

Volhard determinations of the bromine invariably gave slightly lower results; the cause of this was the resinous precipitate, formed when the sample was introduced into silver nitrite solution, which evidently adsorbed some of the bromine.

A resin is also precipitated during determination of bromine in phenyltribromosilane by alkali saponification, but since the sample is refluxed with the alkali solution for 1½ hours the analysis is more accurate.

Diphenyldibromosilane $(C_6H_5)_2SiBr_2$. The fraction with b.p. 175-200° at 12 mm, obtained by fractionation of the crude mixture of phenylbromosilanes, was cut at 12 mm into narrow fractions whose bromine contents were determined.

The bromine content of the 190-194° (12 mm) cut closely approached that of diphenyldibromosilane. This fraction solidified at −70°.

0.2474 g substance: 14.82 ml 0.1 N $AgNO_3$. 0.2460 g substance: 14.88 ml 0.1 N $AgNO_3$ (Volhard). 0.3316 g substance: 4.45 ml 0.5 N KOH. 0.3822 g substance: 4.55 ml 0.5 N KOH (saponification). Found %: Br 46.11, 46.56, 46.64, 47. $C_{12}H_{10}SiBr_2$. Calculated %: Br 46.78.

The identity of this fraction, b.p. 190-194°, with pure diphenyldibromosilane was confirmed by the purity of the diphenylsilanediol which we obtained by hydrolyzing the fraction.

Triphenylbromosilane $(C_6H_5)_3SiBr$. The residue, which boiled at above 200° at 12 mm, was fractionated at 3 mm; between 200 and 220° a colorless crystalline substance came over, m.p. 114-118° (according to the literature $(C_6H_5)_3SiBr$ melts at 118-120°). The bromine content of these crystals (using the saponification method) was 26-27% Br (mean value) (calculated for $(C_6H_5)_3SiBr$ 23.6%). The slightly high bromine content and the slightly low melting point are explained by the lack of purity of the substance. We were unable to recrystallize the triphenylbromosilane because the quantity was insufficient.

In the temperature range of 250-300° (3 mm) we obtained a viscous, red liquid with a mean bromine content of 49%.

General properties of the phenylbromosilanes. Phenylbromosilane and diphenyldibromosilane are heavy, colorless liquids; triphenylbromosilane is a colorless, crystalline substance. All the phenylbromosilanes fume in the air and are readily hydrolyzed by water; they distill in vacuum without decomposition.

SUMMARY

A direct synthesis of methyl- and phenylbromosilanes was effected and the composition of the distilled fractions was investigated.

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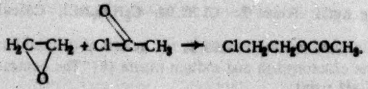
OLEFIN OXIDES

IX. CONDENSATION OF OLEFIN OXIDES WITH NITROSYL CHLORIDE

M. S. Malinovsky and N. M. Medyantseva

We know that olefin oxides react with organic acids to form glycol monoethers, while replacement of the acid by the anhydride leads to diethers. These reactions are well-known [1,2,3] and are exploited on the industrial scale for the production of certain ethers utilized as solvents.

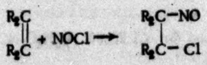
Much less study has been devoted to the reaction between olefin oxides and acid chlorides which, generally speaking, ought to present interest in view of the synthesis of halo-substituted esters containing halogens in the alcohol radical, for example:



Still more neglected have been the reactions of oxides with chlorides of inorganic acids, although the resultant products may be utilized as starting materials for further syntheses.

With the aim of filling this gap, we investigated the action of nitrosyl chloride and carbonyl chloride on the oxides of ethylene, propylene and cyclohexene, and on epichlorhydrin. We report the results in this communication.

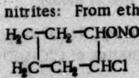
Reactions between nitrosyl chloride and organic compounds may proceed in two directions. First, the whole of the nitrosyl chloride adds on to the substance with which it reacts, undergoing preliminary splitting into NO and chlorine. Double-bond compounds thus usually react with it as follows:



This form of reaction has been closely investigated by N. Ya. Demyanov [2] and pupils.

Second, the nitrosyl chloride simultaneously oxidizes, chlorinates and nitrites the substance. Benzaldehyde is transformed into benzoyl chloride and benzoic acid, while ethyl, isopropyl and butyl alcohols give the corresponding nitrites [5]. Secondary amines react with nitrosyl chloride to form nitrosamines [6]; acetone yields isonitrosoacetone [7], and so on.

Nitrosyl chloride will obviously react with olefinoxides in one of these directions, and most probably in the first; this prediction has been fully confirmed by experiment.

We obtained the following chloralkyl nitrites: From ethylene oxide $ClCH_2CH_2ONO$; from propylene oxide $ClCH_2CH(ONO)CH_3$; from cyclohexene oxide  from epichlorhydrin $ClCH_2CH(ONO)CH_2Cl$.

The structure of the reaction products was confirmed by saponification which gave the corresponding glycol chlorhydrins; the latter were identified as such and also transformed into the α-oxides. Furthermore, some of these esters are described in the literature (they had been prepared by other methods) and their constants agreed fully with those in the literature.

The esters prepared from olefin oxides and nitrosyl chloride possess a characteristic odor which causes headaches.

EXPERIMENTAL

Nitrosyl chloride was prepared from nitrosylsulfuric acid and sodium chloride [8]. Condensation with the oxides was effected in a medium of ether (equal volumes). In these conditions the sole product of condensation is the corresponding ester of nitrous acid, which is formed in good yield. In the absence of ether as a diluent, the yield of nitrous acid ester is considerably reduced due to formation (in many cases) of a certain oily substance containing nitrogen, which does not distill in vacuum and on keeping rapidly decomposes with separation of oxalic acid (when using ethylene oxide and propylene).

1) Condensation of ethylene oxide with nitrosyl chloride. Ethylene oxide (10 g) was diluted with an equal volume of anhydrous ether, and through this mixture (cooled) was passed a stream of nitrosyl chloride until the liquid had acquired a slightly reddish color, which indicated a slight excess of nitrosyl chloride (in the absence of this excess a good deal of the oxide remains unchanged). The mixture was then stood in iced water for 24 hours, following which it was subjected to fractionation. If the mixture had not been allowed to stand for the specified period and distilled quickly or after standing for 2 hours, then a condensation product could not usually be isolated. The oxide and nitrosyl chloride then distill over unchanged.

After distilling off the ether on the water bath from the product which was allowed to stand for 24 hours, the residue was distilled from a small flask with a dephlegmator. A total of 18 g colorless liquid was obtained with b.p. 94-95° at 730 mm (after a second distillation). The yield was 72.5% of the theoretical. Specific gravity 1.2178 (at 20°).

0.2254 g substance: 0.2915 g AgCl. Found %: Cl 32.04. $C_2H_4O_2NCl$. Calculated %: Cl 32.42.

Ethylene chloronitrite had originally been prepared by the action of hydrochloric acid on an aqueous solution of equimolar amounts of ethylene chlorohydrin and sodium nitrite [9] The constants reported for it in the literature are: b.p. 95-96° at 764 mm; d_4^{20} 1.221.

Heating of the ethylene chloronitrite prepared by us with a solution of sodium hydroxide caused ethylene oxide to separate, and sodium nitrite was detected in the solution.

2) Condensation of propylene oxide with nitrosyl chloride. The condensation was performed as above. After the mixture had stood for 24 hours, the ether was distilled off together with unreacted propylene oxide, and the residue fractionally distilled from a flask with a dephlegmator. 11.8 g of liquid was obtained (from 7 g oxide) with b.p. 101-102° at 730 mm, d_4^{20} 1.1214, which fully agreed with the literature data for this compound [9]. The prepared nitrous ester was saponified with potassium carbonate solution to give propylene chlorohydrin with the composition $CH_3CH(OH)CH_2Cl$ (b.p. 128-130°, in agreement with the literature), which confirms the above formula for the nitrous ester.

0.2197 g substance: 0.2573 g AgCl. Found %: Cl 28.90. $C_3H_6O_2NCl$. Calculated %: Cl 28.70.

3) Condensation of cyclohexene oxide with nitrosyl chloride. 7 g cyclohexene oxide (b.p. 129-130°) was condensed with nitrosyl chloride as in the preceding experiments. There was obtained 8 g faintly yellow, oily liquid with b.p. 81-83° at 23 mm, d_4^{20} 1.1468. Yield 64% of the theoretical.

0.2054 g substance: 0.1742 g AgCl. Found %: Cl 21.39. $C_6H_{10}O_2NCl$. Calculated %: Cl 21.70.

Treatment with potassium carbonate solution converted the substance into cyclohexene chlorohydrin; heating with caustic alkali solution led to reformation of cyclohexene oxide, thereby confirming the above formula

4) Condensation of epichlorohydrin with nitrosyl chloride. Condensation was performed with 7 g epichlorohydrin and 9 g $ClCH_2CH(ONO)CH_2Cl$ was obtained or 76% of theory.

The synthesized ester was a colorless liquid with b.p. 72-74° at 42 mm, d^0 1.3434. Careful saponification with weak potassium carbonate solution resulted in formation of $ClCH_2CH(OH)CH_2Cl$, while treatment with caustic alkali gave epichlorohydrin.

0.1974 g substance: 0.3514 g AgCl. Found %: Cl 44.80. $C_3H_5O_2NCl_2$. Calculated %: Cl 44.90.

SUMMARY

1. The reaction between olefin oxides and nitrosyl chloride, which permits the preparation of chloroalkyl nitrites in good yield, was studied.

2. Two new chloroalkyl nitrites were synthesized for the first time.

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Laboratory Organic Chemistry,
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SUGAR DERIVATIVES OF AMINO ACIDS

I. QUINOVOSYL-GLYCINE AND ITS DERIVATIVES

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Carbohydrate-amino acid compounds, which can be regarded as the simplest representatives of the carbohydrate-peptide and carbohydrate-protein complexes, play an important part in biochemical processes and present great interest for biochemistry, biology and chemotherapy.

Carbohydrate-protein complexes enter into the composition of antigens and toxins of microorganisms [1,2]. The specific polysaccharides isolated from microorganisms [2, 3, 4] and also found in higher organisms [5] are carbohydrate-amino acid (peptidic) and monose complexes.

V. G. Drobotko [6], Sh. D. Mashkovsky [7] and others draw attention to the possibility of utilization as medicinal preparations of amino acid analogs, examples of which are synthetic carbohydrate derivatives of amino acids.

In 1949 A. I. Oparin and D. N. Bezinger [8] isolated a high-molecular compound from champagne by dialysis and precipitation with alcohol. Hydrolysis of this compound gave a carbohydrate and a peptide. In the authors' opinion complex compounds are formed in natural wines from amino acids or peptides and sugars with participation of yeasts and their autolyzates. They consider that "these compounds can be extremely diverse in structure, size of complex and bond stability, and their investigation is of undoubted interest for biochemistry because of the demonstrated close connection between these complexes and metabolism."

V. Kretovich and R. Tokareva [9], showed that sugars react with amino acids in various fermentation processes.

Attention was drawn for the first time to the possibility of reaction between sugars and amino acids by the Russian workers S. Kostychev and V. Brilliant [10]. They showed [11] that sugars containing a free reducing group are capable of forming compounds with amino acids and peptides whose carboxyl group permits the formation with copper hydroxide of insoluble precipitates [12]. The carbohydrate-amino acid complexes of S. Kostychev and V. Brilliant are labile and decompose to give the original components. The work of these investigators was continued by N. Ivanov [13].

The work of these and many other investigators made it clear that the reaction of amino acids with sugars involves the amino group of the amino acid and the carbonyl group of the sugar. Further work in this field has been directed toward the synthesis of this type of product.

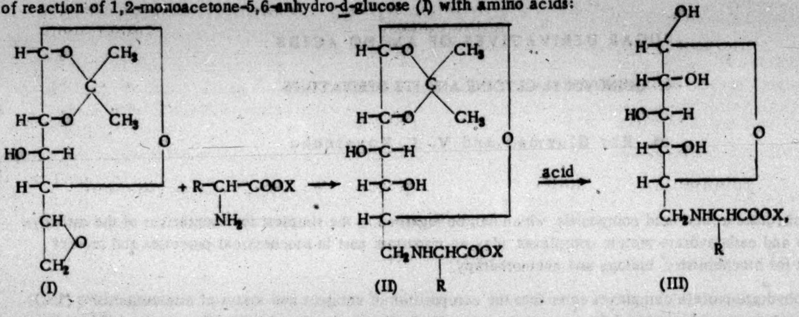
A.M. Kuzin and O.I. Polyakova [1] prepared a glucoside of glycine in the form of the calcium and barium salts. I.C. Irvine [14] synthesized a glucoside of alanine, and A. Stepanov and V. Mameva [15] obtained β-glucosyl-N-lysine.

Some amino acids and peptides have been brought into reaction with glucose or with halogen-containing hexoses and bioses in the form of their ethyl esters [16]. The compounds prepared in this way decompose when saponified [17].

Study of the modes of reaction of carbohydrates with proteins is complex; it is naturally necessary at the start to study the possible modes of interaction of carbohydrates with the simple breakdown products of proteins — amino acids.

The presence in both amino acids and monoses of several functional groups makes possible a whole variety of reactions between them. The hydroxyl group of the sugar might be esterified by the carboxyl group of the amino acid; a link-up may occur through the hydroxyl group of the monose and the hydroxyl (or SH) group of hydroxyamino acids of the type of serine (or cysteine); glucosides of simple sugars may be formed at the cost of the NH_2-, OH- or SH-group of amino acids; finally, those sacchariferous amino acids in which the amino group belongs simultaneously to an amino sugar and an amino acid constitute a special group of substances [18]. The possible diversity of these compounds is evident from the fact that one molecule of a monose can be linked with several identical or different amino acids.

We set ourselves the task of investigating the unusual group of sugar derivatives constituting the products of reaction of 1,2-monoacetone-5,6-anhydro-d-glucose (I) with amino acids:



where R is a radical and X is hydrogen, barium or alkyl.

Consequently we obtain carbohydrate-amino acid compounds which can be regarded as a new group of the simplest representatives of the carbohydrate-peptide and carbohydrate-protein complexes, distinguished by having the nitrogen atom linked with the sixth and not with the first carbon atoms of the monose.

I. Methods of condensation of monoacetone-anhydroglucose with amino acids. The synthesis of the only 6-amino acid derivative of glucose reported in the literature, 6-(N-alanine)-glucose, was described as far back as 1938 by Helferich and Mittag [19], but the problem has not aroused interest since then. The authors condensed anhydroglucose with the ethyl ester of alanine at room temperature, saponified the ester group and the acetone residue, and so obtained 6-(alanine)-glucose in 10% yield.

Utilizing this method we obtained products of condensation of monoacetone-anhydroglucose with the methyl ester of tyrosine, the ethyl ester of p-aminobenzoic acid and the butyl ester of glycine. The method proved to be simple in application, the reaction proceeds in solution and in a melt, and in the presence or absence of pyridine (catalyst). In some cases (cystine), however, the esters of the amino acids are converted during the reaction almost completely into the corresponding derivatives of diketopiperazine and other more complex products [20].

We therefore attempted to carry out the condensation of the anhydroglucose with amino acids, utilizing the observation of A. I. Kiprianov and other workers [21] that aliphatic amino acids are capable of reacting with organic α-oxides. Experiments were performed in melts and in solution, also in presence of a catalyst, but no reaction occurred. Evidently the peculiar structure of this organic oxide here plays a part.

We then developed a new and more convenient method of preparation of sugar derivatives of amino acids, consisting in replacing the free amino acids in the reaction with 1,2-monoacetone-5,6-anhydro-d-glucose by their barium salts, which are usually readily soluble in water and can be prepared by dissolving the amino acids in 0.1-0.2 N barium hydroxide. This method permitted us to prepare monoacetone-quinovose derivatives of various amino acids. Reaction of one mole of the barium salt of an amino acid with two moles of the anhydroglucose gives the bis-(monoacetone-quinovosyl)-N-amino acid.

The pH of the medium is exceptionally important for a successful outcome of the reaction. There are indications that many reactions involving addition to anhydroglucose proceed only in a weakly alkaline medium. Thus, for example, the addition of hydrogen sulfide to anhydroglucose takes place in barium hydroxide solution, and the preparation of 6-alkyl [22] and 6-aryl ethers of monoacetone-glucose [23] is only possible in presence of an alcoholate or phenolate.

Moreover, as shown by G. Lampson and co-workers [24], anhydroglucose reacts readily with disodium phosphate (pH of solution 9.7), whereas no reaction occurs with mono- and trisodium phosphates, due to the strong acidity or alkalinity of the media. The pH of solutions of barium salts is within the range of 8-10, thus being comparable to that of disodium phosphate.

No report has hitherto appeared in the literature on the performance of the reaction between salts of amino acids and organic oxides; we therefore now describe our method: 1-1.2 equivalents of the free amino acid are dissolved in a standard solution of barium hydroxide (0.05-0.2N); solution of the amino acids which we investigated took place in the cold. The solution has an alkaline reaction, due to hydrolysis. Alkalinity is detrimental to the anhydroglucose and is prevented by taking 0.01-0.05 equivalents of barium hydroxide less than is required by calculation.

Addition is made to the solution of the barium salt of the amino acid of 1 equivalent of anhydroglucose which rapidly goes into solution. Flask and contents are immersed in a boiling water bath and refluxed for 1-3½ hours. The solution remains transparent and colorless. At the end of the stated period, addition is made to the hot solution of the calculated amount of 0.4 N sulfuric acid solution in order to remove the barium. The flask contents are shaken for a short period by hand or on a machine until all the carbonate has been converted into barium sulfate. After cooling slowly, the solution filters without special difficulty. The filtrate is tested for freedom from barium, evaporated to dryness in vacuum at a bath temperature not higher than 50-60°, and the product is dried toward the end in a vacuum at 90-95°.

The residue in the flask is the crude product of condensation of the anhydroglucose with amino acids and is often amorphous. The purification procedure will vary with the properties of the amino acid in each particular case. By this method we succeeded in preparing sugar derivatives of such sparingly water-soluble amino acids as tyrosine (1 part dissolves in 2400 parts water) and cystine (1 in 1840 water). In these cases it was necessary to resort to high dilutions of the solution due to the poor solubility of their barium salts.

Bis-monoacetone-quinovosyl derivatives of diamino acids were prepared by reacting two moles of the anhydroglucose with one mole of amino acid.

This method is entirely suitable for preparation of products of condensation of anhydroglucose with di- and polypeptides; for these, however, we must use 0.05 N barium hydroxide solution for dissolving the peptide in order to avoid hydrolysis of the peptide bond.

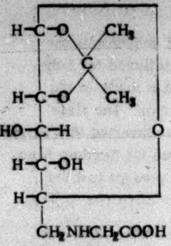
The applicability of this method is not limited to the reactions of anhydroglucose with amino acids; it can be recommended for preparation of derivatives of amino acids with those organic α-oxides which do not undergo hydration in aqueous solution in the course of 3-4 hours. We succeeded, for example, in effecting the reaction between the cystine salt and ethylene oxide, which yielded dihydroxyethyl cystine.

Concerning the cleavage of the acetone residue from monoacetone-quinovosyl-amino acids, this can be effected with the following acids (according to the literature): 0.05-0.1 N sulfuric, hydrochloric, nitric, and acetic acid (in various concentrations from 35% to glacial). The duration and temperature of the reaction vary within very wide limits. After testing the majority of these methods both in the cold and on the water bath, we arrived at the conclusion that all these methods, in their original form, are unsuitable for the present problem. Hydrolysis with 0.1 N sulfuric acid or with acetic acid in the cold or with heating is observed to cause very drastic saponification of the hydrolsis product, and purification is made difficult. We developed a new method of hydrolysis of monoacetone-quinovosyl-amino acids, based on utilization of a hydrogen atmosphere.

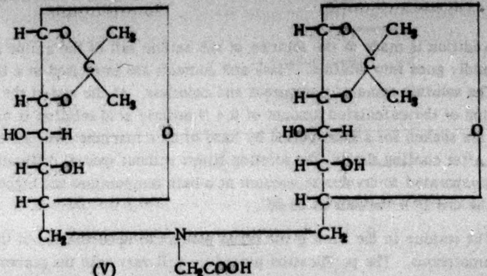
The product of condensation of anhydroglucose with the amino acid is dissolved in 5-10-50 times the volume of 50% acetic acid in a flask fitted with a reflux condenser and a tube reaching to the bottom through which hydrogen is bubbled. Hydrogen is first passed through for a few minutes in order to drive out the air from the flask. The flask is thereupon immersed in a boiling water bath while hydrogen is bubbled steadily for 3-4 hours. During the first 2½ hours the solution remains colorless, but by the end of the heating period the color is faint yellow. The contents are then decolorized with a small quantity of active carbon. The filtrate is evaporated in a vacuum at a bath temperature of 50-60°. After the whole of the liquid has evaporated, addition is made to the flask through the dropping funnel of a few ml distilled water and evaporation is repeated. This operation is repeated 3-4 times until all the acetic acid has been removed. Decolorization with active carbon is repeated at this stage, if necessary, and the liquid is filtered and evaporated in vacuum. The procedure for further purification of the hydrolysis product will vary with the individual case, depending on the solubility and other properties of the prepared substance. This method permitted the cleavage of the acetone residue from the majority of our products of condensation of anhydroglucose with amino acids.

II. Condensation of anhydroglucose with the barium salt of glycine. Reaction between 1,2-monoacetone-5,6-anhydroglucose (I) and amino acids leads to a compound of type (II), cleavage from which of the acetone residue yields a compound of type (III). The name d-quinovosyl -6- has been assigned in the literature to the glucose residue obtained after removal of hydroxyl from the sixth carbon atom: hence compounds (II) and (III) can respectively be named: 1,2-monoacetone-quinovosyl-6-N-amino acid and quinovosyl-6-N-amino acid.

We have prepared monoacetone-quinovosyl-6-N-glycine (IV) and bis-(monoacetone-quinovosyl-6,6')-N-glycine (V):



(IV)

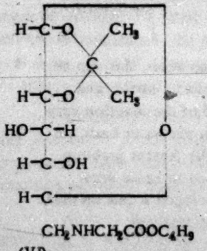


(V)

Substance (IV) was obtained in the crystalline form but (V) was amorphous. Their aqueous solutions are acid to litmus.

It has been reported [23] that 6-substituted esters of monoacetone-glucose are formed when carboxylic acids are heated with anhydroglucose to 140°. Esters with acetic and benzoic acids were thus prepared. It would thus be expected that also in the condensation of anhydroglucose with amino acids the amino acid residue would combine at the carboxyl group. We performed the condensation of anhydroglucose with the butyl ester of glycine for the purpose of demonstrating that our reaction between anhydroglucose and the barium salts of amino acids does not involve addition of the amino acid residue to the carboxyl group attached to the ethylene oxide ring.

In our case the addition indisputably takes place at the amino group, since the carboxyl group is esterified. The obtained compound (VI) gives, on saponification with barium hydroxide, a small yield of product (IV).



(VI)

Compound (IV), prepared by condensation of anhydroglucose with the barium salt of glycine, and the substance synthesized with the help of the butyl ester of glycine proved to be identical (in melting point, nitrogen content, specific rotation and chemical properties). Hence by using the barium salts of amino acids for the reaction with anhydroglucose we have the possibility of preparing compounds of the type of (IV) and (V).

After cleavage of the acetone residue from compounds (IV) and (V), quinovosyl-6-N-glycine and diquinovosyl 6,6'-N-glycine are isolated.

Both compounds are dextrorotary, whereas their 1,2-monoacetone derivatives are levorotatory. Their aqueous solutions do not undergo mutarotation. These glycine derivatives are readily oxidized in an acid solution even with atmospheric oxygen. They are probably decomposed into their components. Glucose gives rise to 5-hydroxymethylfurfural, which with amino acids gives colored products whose amount is smaller in a solution of diquinovosyl-amino acids.

In this respect there is full agreement with the data of M. Wolfrom [25] who observed that heating of amino acids with glucose in acid solution gave an amount of colored substances smaller than in the case of N-disubstituted amino acids.

EXPERIMENTAL

Reaction of Anhydroglucose with Glycine

1. a) Condensation of the anhydroglucose with barium salt of glycine. The monoacetone-glucose required for the investigation was prepared by the procedure of Zervas and Sessler [26] as modified by Gluzman and Litvinenko [27]. 6-p-Tosyl-monoacetone-glucose was prepared by A. Meyer's method [28] and then the anhydroglucose by the method of Ohle and Varga [29]. In the last two stages dichloroethane was substituted for chloroform without fall in yields.

1.1 g (14.6 millimoles) glycine is dissolved, by heating on the water bath, in 67.8 ml 0.2 N barium hydroxide. To the solution is added 2.78 g (13.6 millimoles) anhydroglucose. Further treatment is as described in the general account of the method above. After heating for 2½ hours the barium is precipitated with sulfuric acid (36.1 ml), and the residue after evaporation in vacuum and drying at 90-100° is digested with 10-15 ml dry ethyl acetate and then with acetone; the product is filtered and the residue on the filter is washed with acetone and dry ether. Yield 2.48 g (85% of the theoretical). The substance melts at 173-174° without decomposition. The aqueous solution of the prepared glycine derivative has an acid reaction; it readily dissolves barium carbonate and the barium can only be precipitated from it with sulfuric acid, and not with carbon dioxide.

$[\alpha]_D^{22}$ −6.3° (c = 2.922; water).

0.1467 g substance: 5.17 ml 0.1 N H_2SO_4. 0.1659 g substance: 5.90 ml 0.1 N H_2SO_4. Found %: N 4.93, 4.98. $C_{11}H_{19}O_7N$. Calculated %: N 5.04.

The prepared 1,2-monoacetone-quinovosyl-6-N-glycine is readily soluble in water and in dilute and glacial acetic acid; it is less soluble in the cold in 70% alcohol but readily dissolves when heated. The product is insoluble in dry acetone, ethyl acetate, benzene and dichloroethane. A white silver salt can be got from the aqueous solution by the usual method.

b) Hydrolysis of 1,2-monoacetone-quinovosyl-6-N-glycine. 2 g condensation product is hydrolyzed with 50 ml 50% acetic acid in a hydrogen atmosphere for 3 hours by the above-described method. The residue in the flask (1.2 g) is evaporated down and recrystallized from 50 ml absolute alcohol, and the crystals are washed with absolute methanol and dry ether. Yield 0.5 g (29% of the theoretical); m.p. 133-135°. Quinovosyl-6-N-glycine is soluble in water, dilute and glacial acetic acid, and methanol; it is insoluble in benzene, ether and dichloroethane; it readily reduces Fehling solution when heated on the boiling water bath.

$[\alpha]_D^{14}$ +30.8° (c = 0.973; water).

0.1534 g substance: 6.24 ml 0.1 N H_2SO_4. 0.1408 g substance: 5.78 ml 0.1 N H_2SO_4. Found %: N 5.69, 5.74. $C_8O_{15}H_7N$. Calculated %: 5.90.

Quinovosyl-6-N-glycine was characterized by the preparation of its phenylosazone. 0.1 g of the substance and 0.2 g phenylhydrazine are dissolved in 5 ml water and 0.3 ml 50% acetic acid. The solution is heated on the water bath for 1 hour. Toward the close of the heating a brownish substance forms on the walls of the vessel. The solution is allowed to stand overnight, the crystals are filtered and washed with 10% acetic acid, water, toluene and ether. Yield 0.07 g. M.p. of the phenylosazone 149°.

2. a) Condensation of 2 moles anhydroglucose with the barium salt of glycine. 0.39 g (5.2 millimoles) glycine is dissolved by heating in 24 ml 0.2 N barium hydroxide. To the solution is added 2.1 g (10.3 millimoles) anhydroglucose; heating for 2½ hours. The barium is precipitated with 12.2 ml 0.4 N sulfuric acid. Further treatment is as in the previous case. The residue in the flask is digested with ethyl acetate and then with acetone (20 ml), filtered, washed with dry ether and dried in vacuum. M.p. 168-169°. Yield 1.25 g (50.2% of the theoretical).

$[\alpha]_D^{18}$ −8.2° (c = 1.439; water).

0.2134 g substance: 4.09 ml 0.1 N H_2SO_4. 0.1588 g substance: 3.25 ml 0.1 N H_2SO_4. Found %: N 2.68, 2.87. $C_{20}H_{33}O_{12}N$. Calculated %: N 2.92.

The prepared bis-(monoacetone-quinovosyl-6,6″)-N-glycine is readily soluble in water and in aqueous and glacial acetic acid. The aqueous solution is acid to litmus and dissolves barium carbonate. The compound does not reduce Fehling solution.

b) Hydrolysis of bis-(monoacetone-quinovosyl-6,6″)-N-glycine. 1.5 g of the compound is dissolved by heating for 3 hours with 38 ml 50% acetic acid in a hydrogen atmosphere; further treatment as for the monosubstituted glycine. Yield of crude product 0.75 g (59% of the theoretical). The substance is successively digested with 15 ml absolute ethanol and 12 ml absolute methanol; it is then washed on the filter with absolute methanol and dry ether. Yield 0.25 g (19.2% of the theoretical). An additional 0.2 g product is recovered from the combined alcoholic filtrates after decolorization with active carbon and evaporation at room temperature. The synthesized product decomposes at 110-120° and is a white substance readily soluble in water, 50% methanol, ethanol, isopropanol; poorly soluble in other organic solvents; it readily reduces Fehling solution when heated. It also gives a positive reaction for a free carboxyl group (formation of salts). It does not form a color with an aqueous solution of ninhydrin.

$[\alpha]_D^{22}$ +23.8° (c = 0.911; water).

0.1840 g substance: 4.68 ml 0.1 N H_2SO_4. 0.1224 g substance: 3.03 ml 0.1 N H_2SO_4. Found %: N 3.56, 3.47. $C_{14}H_{25}O_{12}N$. Calculated %: N 3.50.

3. a) Condensation of 1,2-monoacetone-5,6-anhydro-d-glucose with the n-butyl ester of glycine. To a warm solution of 1.55 g (7.6 millimoles) anhydroglucose in 15 ml dry dichlorethane is added 1.6 g (12 millimoles) butyl ester of glycine prepared by Abderhalden's method [30]. The mixture is well stirred and heated to 60-70°. A pale yellow solution is formed which is allowed to stand for 3 days at room temperature.

At the expiration of this period the dichlorethane and excess butyl ester are distilled off at 3-4 mm at a bath temperature of 100°. The oil remaining in the flask is heated with 16 ml distilled water on a water bath for 3 hours under a reflux condenser. During this treatment the residual butyl ester of glycine is partly converted into diketopiperazine which dissolves in the water, while the glucose derivative remains in the form of a viscous oil. After separating the aqueous solution, the residue is worked up 6 times with 15-20 ml lots of chloroform. The combined chloroform extracts are decolorized with active carbon and dried with sodium sulfate prior to distillation of the solvent. The product is a faint-yellow, amorphous, very hygroscopic substance with a softening temperature of 50-60°; it is readily soluble in chloroform, acetic acid, and methanol, less readily soluble in dichlorethane and acetone. Water precipitates it from methanol solution as a viscous oil. Yield of n-butyl ester of 1,2-monoacetone-quinovosyl-6-N-glycine 2.3 g (90% of the theoretical).

$[\alpha]_D^{22}$ +14.6° (c = 1.732; dry chloroform).

0.1374 g substance: 3.92 ml 0.1 N H_2SO_4. 0.1968 g substance: 5.76 ml 0.1 N H_2SO_4. Found %: N 3.99, 4.10. $C_{15}H_{27}O_7N$. Calculated %: N 4.20.

The condensation of the anhydroglucose with the equivalent amount of butyl ester of glycine can be performed by heating the solution on the water bath. Formation of diketopiperazine cannot then be observed. The same results can be achieved by performing the condensation in a mixture of dichlorethane and dry methanol (8:1). Large amounts of methanol might result in formation of 1,2-monoacetone-6-methylglucose, which contaminates the main product.

b) Hydrolysis of the butyl ester of 1,2-monoacetone-quinovosyl-6-N-glycine. 2.5 g of the butyl ester is dissolved by heating in 200 ml 0.2 N barium hydroxide solution (3 equivalents). The solution is left at room temperature for 6 hours, after which the barium is precipitated with sulfuric acid. After evaporation in vacuum of the filtrate (following decolorization with active carbon), the residue is a colorless, amorphous, hygroscopic substance. The product of hydrolysis is dissolved in 10 ml dry acetone by heating and the solution seeded with the product of condensation of the anhydroglucose with glycine prepared via the barium salt of glycine. The acetone solution is left for 5-6 days, in the course of which crystals come down which are repeatedly triturated with 10 ml dry acetone. Yield of crystalline product 0.5 g (24% of the theoretical). Evaporation of the acetone filtrates leaves an amorphous substance with the same nitrogen content as the crystalline product. M.p. of the crystalline product 173-175° (without decomposition). The crystalline product did not depress the melting point of the product of condensation of the anhydroglucose with glycine (prepared via the barium salt).

$[\alpha]_D^{23}$ −7.8° (c = 2.29; water).

0.1750 g substance: 6.20 ml 0.1 N H_2SO_4. 0.1860 g substance: 6.76 ml 0.1 N H_2SO_4. Found %: N 4.96, 5.08. $C_{11}H_{19}O_7N$. Calculated %: N 5.04.

The aqueous solution of 1,2-monoacetone-quinovosyl-6-N-glycine, prepared via the butyl ester of glycine, has an acid reaction to litmus, which points to the presence of a free carboxyl group; it gradually dissolves barium carbonate.

SUMMARY

1. The literature on carbohydrate-protein and -peptide complexes is briefly surveyed and attention is drawn to the importance of these substances in biology, biochemistry and chemotherapy.

2. A new and convenient method is developed for the preparation of a group of sugar derivatives of amino

acids in which the sixth carbon atom of a monose is linked to the amino acid through the nitrogen atom of the amino group. The method involves condensation of monoacetone-anhydroglucose with barium salts of amino acids.

3. Monoquinovosyl-6- and diquinovosyl-6,6'-N-glycines and their acetone derivatives have been prepared, as well as the butyl ester of monoacetone-quinovosyl-6-N-glycine.

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N-BROMO(CHLORO)-N'-ARYLSULFONYL QUINONEDIIMINES

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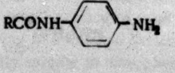
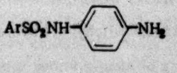
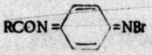
Some new substituted quinoneimines were described in previous papers, namely: quinonebromoimides and quinonedibromodiimides [1,2], quinonediiododiimides [3], N-arylsulfonyl quinoneimines [4], and N-arylsulfidyl quinoneimines [5].

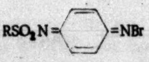
On the basis of the reaction of formation of quinonebromoimides and quinonedibromodiimides one of us has described a sensitive reaction for p-diamines, p-aminophenols and alkyl ethers of the latter [1,6]. Observations on the quinonebromoimide reaction have shown that N-acetyl(benzoyl)-1,4-phenylenediamine (Formula I) does not undergo the quinonebromoimide reaction, whereas N-arylsulfonyl-1,4-phenylenediamine (Formula II) exhibits an intense quinonebromoimine reaction. These facts prompted us to study the action of bromine and hypobromites on substituted p-phenylenediamines. It transpired that an alkaline solution of hypobromite acts on N-acetyl-1,4-phenylenediamine (Formula I; R = CH$_3$) to give a compound in the form of small yellow needles. Attempts to isolate the reaction product in the pure form were unsuccessful; the new compound rapidly changes in composition.


(I)


(II)

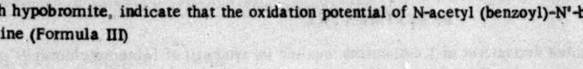
A more stable product is formed, however, by the action of hypobromite on N-arylsulfonyl-1,4-phenylenediamine. Evidently the absence of the quinonebromoimide reaction with N-acetyl (benzoyl)-1,4-phenylenediamine and its occurrence with N-arylsulfonyl-1,4-phenylenediamine, as well as the great stability of the product of reaction with hypobromite, indicate that the oxidation potential of N-acetyl (benzoyl)-N'-bromo-1,4-benzoquinonediimine (Formula III) is considerably higher than that of N-arylsulfonyl-N'-bromo-1,4-benzoquinonediimine (Formula IV).


(III)


(IV)

A more convenient route to the latter compounds was found, however, in the action of bromine on a substituted phenylenediamine in acetic acid solution, followed by dilution with water. In this paper we describe the N-bromo-(chloro)-N'-arylsulfonyl-quinonediimines which have not previously been described in the literature.

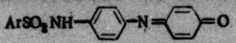
The synthesized N-bromo(chloro)-N'-arylsulfonyl-1,4-quinonediimines are crystalline substances with a yellow color. They differ from the quinone dibromodiimides and quinonebromoimides in being fairly stable in the pure form at the ordinary temperature and in possessing sharp melting points. They decompose, usually with gas evolution, at a much higher temperature than their melting point. The N-bromo(chloro)-N-arylsulfonyl-quinonediimines, which we investigated, quantitatively liberate iodine from acidic solutions of iodides according to the equation:



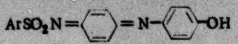
This reaction was utilized for determination of the oxidation equivalent of these compounds, and, consequently, for their identification.

In alkaline solution the new compounds readily react with phenols and very deep blue solutions are obtained from which dark-red indophenols separate on acidification. A qualitative test revealed the presence

of sulfur in these indophenols. Quantitative determination of sulfur indicates that the structure of the indophenols corresponds to formula (V) or (VI):



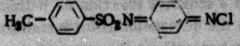
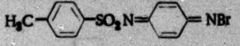
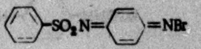
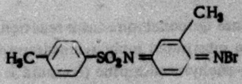
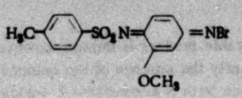
(V)



(VI)

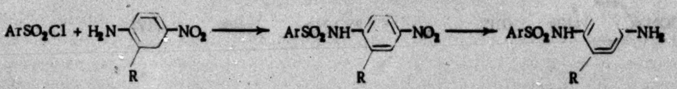
The prepared compounds are set forth in the table.

TABLE

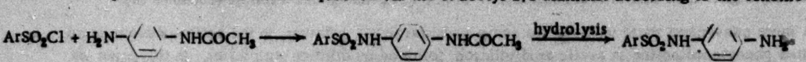
No.	Name	Formula	M.p.
1	N-Chloro-N'-p-toluenesulfonyl-1,4-benzoquinonediimine		93.1*
2	N-Bromo-N'-p-toluenesulfonyl-1,4-benzoquinonediimine		144.5
3	N-Bromo-N' benzenesulfonyl-1,4-benzoquinonediimine		132
4	N-Bromo-N^5-p-toluenesulfonyl-2,5-toluquinonediimine . .		47
5	N^4-Bromo-N^1-p-toluenesulfonyl-2-methoxy-1,4-benzoquinonediimine		83.5

EXPERIMENTAL

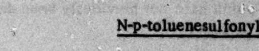
The N-arylsulfonated derivatives of 1,4-diamines required for synthesis of N-bromo(chloro)-N'-arylsulfonyl-quinonediimines were prepared in part according to the scheme:



In some cases it proved more convenient to proceed via the N-acetyl-1,4-diamines according to the scheme:



N-p-toluenesulfonyl-1,4-phenylenediamine



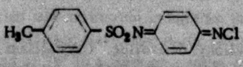
Preparation was by reduction of N-toluenesulfonyl-4-nitroanilide. The latter was synthesized by the action of toluenesulfochloride on 4-nitroaniline in acid solution. 55.2 g (0.4 mole) 4-nitroaniline was suspended in 200 ml xylene and 42.4 g calcined sodium carbonate (0.4 mole or a twofold excess) was added. The mixture was refluxed in a flask fitted with a stirrer and placed on a sand bath. p-Toluenesulfochloride (76.2 g; 0.4 mole) was added in portions to the boiling mixture. The completion of the reaction was indicated by disappearance of the reaction for 4-nitroaniline; this necessitated addition of an additional excess of toluenesulfochloride; heating was continued for 4 hours. The xylene was then distilled off with steam and the residue in the flask was extracted with 1 liter 3.5% sodium hydroxide solution. This effected separation from a by product, di-p-toluenesulfonyl-4-nitroanilide, which is insoluble in alkali. The alkali solution, after filtration from insoluble residue, was acidified with hydrochloric acid; the precipitate was filtered, washed with water and dried.

After washing with alcohol the precipitate had m.p. 189.6° (corrected, like all the other melting points.) After two recrystallizations the m.p. was 193°. The literature gives the m.p. of toluenesulfonyl-4'-nitroanilide as 191° [7]. Yield 73.5 g, or 63% of the theoretical.

The nitro product was reduced with hydrosulfite in an alkaline medium. For this purpose, 73.0 g (0.25 mole) was dissolved in 1300 ml 3.5% NaOH, and at a temperature of 50-60° hydrosulfite was added until the reaction mass was decolorized. The filtered and cooled solution was then exactly neutralized with hydrochloric acid. The precipitate was filtered at the pump, washed with water, and dried. Yield 57.2 g 87.3% of the theoretical. M.p. 178.5° (unrecrystallized).

According to the literature [8] N-p-toluenesulfonyl-1,4-phenylenediamine melts at 186°.

N-Chloro-N'-p-toluenesulfonyl-1,4-benzoquinonediimine

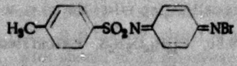


To 220 ml 0.2 N hypochlorite solution, prepared by passing chlorine gas into sodium hydroxide solution, was added at 0° (ice cooling) 4 g N-p-toluenesulfonyl-1,4-phenylenediamine in 25 ml 5% hydrochloric acid. The yellow precipitate was filtered and dissolved in dichloroethane. A portion of the dichloroethane was distilled off in vacuum and a small amount of ethyl alcohol was added to the residue. Small yellow needles crystallized out. M.p. (after drying in a vacuum desiccator) 93.1°. The yellow crystals are stable in ordinary conditions for several days. Readily soluble in ether, benzene and dichloroethane, poorly soluble in alcohol, soluble in water. In an ammoniacal medium it forms a deep-blue color with phenol and a blue-violet color with 1-naphthol.

The product was analyzed by determination of the oxidation equivalent. A weighed amount of the quinonediimine was dissolved in alcohol, an excess of KI solution was added and the mixture acidified with 10% H_2SO_4. The separated iodine was titrated with thiosulfate.

0.0624 g substance: 8.45 ml 0.1 N $Na_2S_2O_3$. 0.1000 g substance: 13.68 ml 0.1 N $Na_2S_2O_3$. Found: equiv. 73.94, 73.11. $\frac{1}{4}$ $C_{13}H_{11}O_2N_2ClS$. Calculated: equiv. 73.68. 0.1609 g substance: 0.1243 g $BaSO_4$ (Carius). Calculated %: S 10.63. $C_{13}H_{11}O_2N_2Cls$. Calculated %: S 10.68.

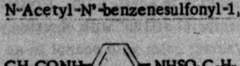
N-Bromo-N'-p-toluenesulfonyl-1,4-benzoquinonediimine



A solution of N-toluenesulfonyl-1,4-phenylenediamine in glacial acetic acid is added to a solution of bromine in glacial acetic acid, cooled to 0°. 3 moles bromine is taken for each mole of amine (i.e., a 50% excess). The mixture is carefully stirred and poured into cold water. The precipitate is filtered at the pump and washed with ethyl alcohol, prior to recrystallization from dichloroethane with addition of some gasoline. Dark yellow crystals, m.p. 144.5°. Less stable than the chloro derivative. Analysis shows presence of halogen and sulfur. Readily soluble in benzene, xylene and dichloroethane, difficultly soluble in alcohol. It rapidly decomposes in alkaline solutions. In an ammoniacal medium it gives a deep blue color with phenol and blue-violet with 1-naphthol. It was analyzed by determination of the oxidation equivalent (as detailed above).

0.0716 g substance: 8.50 ml 0.1 N $Na_2S_2O_3$. 0.0820 g substance: 9.72 ml 0.1 N. $Na_2S_2O_3$. Found: equiv. 84.29, 84.47. $\frac{1}{4}$ $C_{13}H_{11}O_2N_2BrS$. Calculated: equiv. 84.80.

N-Acetyl-N'-benzenesulfonyl-1,4-phenylenediamine



This compound is used for the preparation of N-benzenesulfonyl-1,4-phenylenediamine by the second scheme. It was synthesized by treating N-acetyl-1,4-phenylenediamine with benzenesulfochloride in presence of sodium carbonate in suspension in xylene. Reaction temperature 70°. After distilling off the xylene and extracting the unreacted N-acetyl-1,4-phenylenediamine with hot water, the product was crystallized from alcohol and melted at 157°. Pinkish needles. Yield 40 g (74.4% of the theoretical). Not described in the literature.

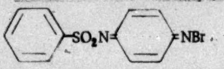
0.1484 g substance: 01197 g $BaSO_4$ (Carius). Found %: S 11.04. $C_{14}H_{14}O_3N_2S$. Calculated %: S 11.0

N-Benzenesulfonyl-1,4-phenylenediamine was prepared from the acetyl derivative by hydrolysis in alkaline solution. 40 g acetyl derivative (0.137 mole) was dissolved in 150 ml caustic alkali solution containing 12 g (0.3 mole) sodium hydroxide.

After heating for 6 hours on the water bath, the excess alkali was precisely neutralized with hydrochloric acid until the reaction to litmus was neutral. The white precipitate was recrystallized from alcohol. The obtained N-benzenesulfonyl-1,4-phenylenediamine has m.p. 170.5°.

The literature gives m.p. 173° [8]. Yield 20 g or 58.5% of the theoretical. It gives the quinonebromoimide reaction; procedure is described in [6].

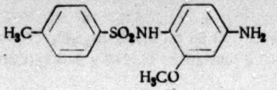
N-Bromo-N'-benzenesulfonyl-1,4-benzoquinonediimine



The preparation was similar to that of the corresponding toluenesulfonyl derivative. Crystallization from dichloroethane with addition of alcohol gave dark yellow crystals with m.p. 132.0°. Sulfur and halogen are present. Readily soluble in benzene, xylene and dichloroethane. Gives a blue color with phenol in an ammoniacal medium and a violet one with 1-naphthol. It quantitatively liberates iodine from acidified solutions of iodides. Analysis was performed by determination of the oxidation equivalent by titrating the separated iodine with thiosulfate.

0.0605 g substance: 7.51 ml 0.1 N $Na_2S_2O_3$. 0.1032 g substance: 3.05 ml 0.1 N NaS_2O_3. Found: equiv. 80.67, 79.33. $\frac{1}{4}$ $C_{12}H_9O_2N_2BrS$. Calculated: equiv. 81.3. 0.1600 g substance: 0.1402 g $BaSO_4$ (Carius). Found %: S 9.56. $C_{12}H_9O_2N_2BrS$. Calculated %: S 9.81.

5-Amino-2-p-toluenesulfaminoanisole



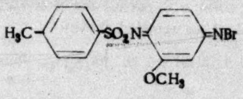
Prepared by reduction of 5-nitro-2-p-toluenesulfaminoanisole with hydrosulfite in an alkaline medium in a similar manner to the preparation of N-p-toluenesulfonyl-1,4-phenylenediamine. Reaction temperature 50-70°. A single crystallization gives colorless needles, m.p. 166°. Repeated crystallization raises the m.p. to 172.5°.

0.3000 g substance: 20.55 ml 0.1 N HCl (Kjeldahl). Found %: N 9.60. $C_{14}H_{16}O_3N_2S$. Calculated %: N 9.58.

In addition titration was performed with sodium nitrite (using the preparation with m.p. 166°).

0.3354 g substance: 11.6 ml 0.1 N $NaNO_2$. 0.4287 g substance: 15.0 ml 0.1 N $NaNO_2$. Found: equiv. 286.3, 286.2. $C_{14}H_{16}O_3N_2S$. Calculated: equiv. 292.3.

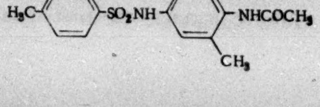
N^4-Bromo-N^1-p-toluenesulfonyl-2-methoxy-1,4-benzoquinonediimine



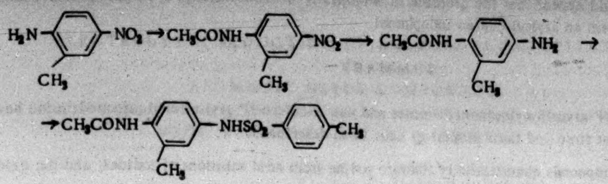
Prepared by the action of bromine on the preceding compound in solution in acetic acid. Crystallization from dichloroethane gave a yellow precipitate with m.p. 83.5°. It decomposes at 135° with charring and evolution of a red vapor. Readily soluble in organic solvents. Gives a blue (azure) color with phenol in an ammoniacal medium; with 1-naphthol the color is dark blue. The compound was analyzed by determination of the oxidation equivalent.

0.1220 g substance: 13.35 ml 0.1 N $Na_2S_2O_3$. 0.1182 g substance: 12.82 ml 0.1 N. $Na_2S_2O_3$. Found: equiv. 92.17, 91.58. $\frac{1}{4}$ $C_{14}H_{13}O_3N_2BrS$. Calculated: equiv. 92.28. 0.1602 g substance: 0.0966 g $BaSO_4$ (Carius). Found %: S 8.55. $C_{14}H_{13}O_3N_2BrS$. Calculated %: S. 8.69.

2-Acetamido-5-p-toluenesulfaminotoluene



The acetyl product necessary for preparation of the 2-amino-5-p-toluenesulfaminotoluene was prepared according to the following scheme:

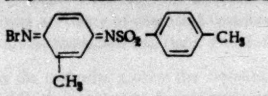


The procedure differed from that in the case of N-acetyl-N'-benzenesulfonyl-1,4-phenylenediamine in that the reaction was performed in aqueous solution. 10.6 g sodium carbonate (0.1 mole) was dissolved in 200 ml water and addition was made to the solution of 16.52 g (0.1 mole) 5-amino-2-acetylaminotoluene. The mixture was heated to 70° in a flask on a water bath fitted with a stirrer and a reflux condenser. With energetic stirring at the specified temperature addition was made in small portions of 19 g (0.1 mole) p-toluenesulfochloride. After 4 hours the precipitate was filtered, washed with water and recrystallized from alcohol. Light pink needlets, m.p. 166°. Not described in the literature.

0.1616 g substance: 0.1228 g $BaSO_4$ (Carius). Found %: S 10.44. $C_{16}H_{18}O_3N_2S$. Calculated %: S 10.07.

It does not give the quinonebromimide reaction. It is more difficultly soluble in organic solvents than the corresponding amine. Hydrolysis of the acetyl derivative with caustic alkali gives the corresponding amine. After crystallization from alcohol the amine has m.p. 127.5°. It gives the quinonebromimide reaction. It is not described in the literature.

N^2-Bromo-N^5-p-toluenesulfonyl-2,5-toluquinonediimine



Prepared by the action of bromine on 5-amino-2-p-toluenesulfamidotoluene. After crystallization from dichloroethane (precipitation with alcohol) it forms a light yellow precipitate. M. p. 47°. Decomposes violently at 170°. It is readily soluble in dichloroethane and benzene, less readily soluble in alcohol, insoluble in water. With phenol in an ammoniacal medium and with 1-naphthol it forms a deep blue color. It liberates iodine from acidified iodide solutions.

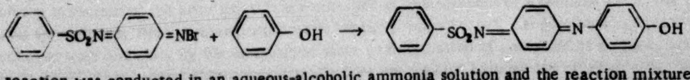
Analysis was effected by determination of the oxidation equivalent and by Carius determination of sulfur.

0.0454 g substance: 5.2 ml 0.1 N $Na_2S_2O_3$. 0.1236 g substance: 14.12 ml 0.1 N $Na_2S_2O_3$. Found: equiv. 87.58, 87.56. $\frac{1}{4}$ $C_{14}H_{13}O_2N_2BrS$. Calculated: equiv. 88.06. 0.1600 g substance: 0.1042 g $BaSO_4$ (Carius). Found %: S 8.95. $C_{14}H_{13}O_2N_2BrS$. Calculated %: S 9.11.

Study of the indophenol reaction of N-bromo-N'-benzenesulfonyl-1,4-benzoquinonediimine

There are indications in the literature that joint oxidation with hypochlorite of N-p-toluenesulfonyl-1,4-phenylenediamine and phenols leads to formation of arylsulfonated indophenols [9]. We have attempted to prepare a similar compound by reaction of N-bromo-N'-benzenesulfonyl-1,4-benzoquinonediimine with phenol.

The proposed reaction should proceed according to the scheme:



The reaction was conducted in an aqueous-alcoholic ammonia solution and the reaction mixture was treated with benzene; the benzene layer was removed and contained the unreacted phenol and quinonediimine; the indophenol was extracted from the aqueous layer with butyl alcohol. Evaporation of the butyl alcohol at low temperature left a resinous material, fromwhich the indophenol was extracted with dilute ammonia solution. The filtered solution was acidified with acetic acid. The resultant dark flocs acquired a deep violet color after drying and melted unsharply with preliminary sintering at 188°. All attempts to crystallize the material from a solvent were unsuccessful, so that analysis was performed on the crude product.

0.1587 g substance: 0.1086 g $BaSO_4$ (Carius). Found %: S 9.40. $C_{18}H_{14}O_3N_2S$. Calculated %: S 9.47.

Consequently it would appear that the bromine in N-bromo-N'-benzenesulfonyl-1,4-benzoquinonediimine reacts with phenols to form an arylsulfonated indophenol.

SUMMARY

1. Four N-bromo-N'-arysulfonylquinonediimines and one N-chloro-N'-arylsulfonylquinonediimine have been prepared for the first time and their properties have been described.

2. The prepared compounds quantitatively liberate iodine from acid solutions of iodides, and the oxidation equivalent is found to be one-quarter of the molecular weight.

3. The reaction of N-bromo-N'-benzenesulfonyl-1,4-benzoquinonediimine with phenol in an ammoniacal medium is described; it forms an indophenol containing sulfur.

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Ivanov Institute of Chemical Technology

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* See Consultants Bureau translation, p. 1917.

** See Consultants Bureau translation, p. 1059.

*** See Consultants Bureau translation, p. 1053.

**** See Consultants Bureau translation, p. 1901.

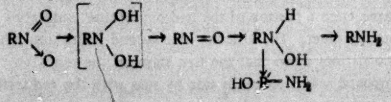
ELECTROLYTIC REDUCTION OF HALOALKYL-SUBSTITUTED AROMATIC NITRO COMPOUNDS

V. M. Berezovsky and V. S. Varkov

The utilization of noble metals as catalysts in the reduction of haloalkyl-substituted aromatic nitro compounds permits the reaction to be carried out in a medium of inorganic or organic acid or in a neutral medium, i.e., in conditions favoring the formation of primary amines and replacement of an atom of chlorine by hydrogen. Catalysts of nonnoble metals must be used in an alkaline or neutral medium. One of us has shown [1] that the process of alkaline reduction of 2-chloro-methyl-4-nitrotoluene in specially selected, narrowly maintained, reaction conditions can be directed in such a manner that the main reaction product is a primary amine; during the reaction the chlorine atom is eliminated. By this method the hydrogenation of 2-chloromethyl-4-nitrotoluene in alcoholic alkaline medium with a skeletal Ni catalyst gives o-4-xylidine in 50-70% yield. This reaction is accompanied, however, by other reactions which are characteristic of alkaline reduction and which become the predominant reactions if the conditions deviate from those selected; in such cases azoxy compounds and other products of alkaline reduction are formed. More consistent reductions to the primary amine were only obtained by using high dilutions (60- to 80-fold) of the starting substance.

With the objective of establishing more favorable conditions for formation of the primary amine and for elimination of the chlorine atom from the aliphatic substituent, we employed electrolytic processes which are widely used for effecting a variety of chemical transformations of organic compounds, e.g., the stepwise reduction of nitro compounds, various oxidation reactions, introduction of halogens into molecules, and even for nitrations [2], etc.

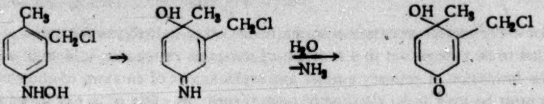
During the cathodic process the aromatic nitro compound is initially reduced to the dihydroxamine [3] which is then dehydrogenated to the nitrosocompound; this reaction takes place at high velocity. In the next stage of the process the nitroso compound is readily reduced to arylhydroxylamine. In an alkaline or neutral medium the latter compound undergoes further reduction very slowly and chemical condensation processes predominate in the first stage. Reduction of arylhydroxylamines in an acid medium proceeds at an adequately high velocity (although still more slowly than its rate of formation from the nitroso compound), thereby avoiding chemical condensation processes, and leads to formation of primary amine in high yield when a suitable metal is selected for the cathode. The acidic reduction of aromatic nitro compounds may be represented by the following scheme:



The halogen of the nucleus is not substituted by hydrogen by the electrochemical route [4], and only one nitro group is reduced in chloronitro compounds, e.g., from p-chloronitrobenzene we obtain p-chloroaniline and from chlorodinitrobenzene we obtain chloronitroaniline. These facts demonstrate the negative influence of the halogen of the aromatic nucleus on the reduction of the nitro group of this ring. In certain conditions of electrolytic reduction the reduction of the nitro group is accompanied by replacement of a chlorine atom, not by hydrogen but by hydroxyl; for instance, from p-chloronitrobenzene we get p-aminophenol. Reduction of aliphatic nitro compounds proceeds with difficulty by the electrolytic route with formation of a mixture of products with a lower degree of chlorination, while methyl chloride practically does not split off halogen [4]. Carbon tetrachloride is not reduced at a platinum cathode, while at a copper and lead cathode reduction takes place only with formation of chloroform. It is therefore clear that it is much more difficult to reduce the chlorine atom than it is to reduce the nitro group, all the more since the results of electrolysis depend in high degree on the magnitude of the overvoltage, the concentration of the substance which is being reduced and other experimental conditions.

In this investigation we have studied the effect of various factors (composition of the medium, the material of the cathode, the temperature, the current density, etc.) on the formation and yield of o-4-xylidine by electrolytic reduction of 2-chloromethyl-4-nitrotoluene. In this process it is possible to employ as the catholyte solutions of the substance in aqueous ethyl alcohol [5] and acetic acid [6]. We have shown, however, that there are considerably greater advantages in utilizing 2-chloromethyl-4-nitrotoluene in the form of a suspension.

A small amount of ammonia is found to be evolved when the xylidine is distilled off from the neutralized electrolytic solutions. This may be accounted for on the basis of the following mechanism of the side reaction proceeding during acidic reduction. During the second part of the cathodic process, when the arylhydroxylamine has already been formed, the latter is rearranged under the influence of sulfuric acid to form a quinolimine containing a quinoid nitro group; this imino group is hydrolyzed by acid with formation of ammonia, and at the same time is replaced by oxygen:

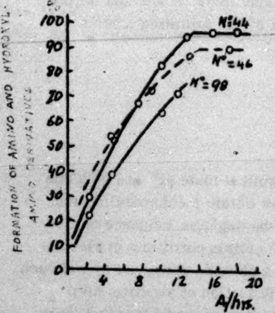


The final product of this rearrangement and hydrolysis is quinol. The proposed reaction mechanism is consistent with known data for p-tolylhydroxylamine [7]. The observed decrease in yield of primary amine with rising current density, which is associated with electric and thermal phenomena, may also be governed by the intensification of this side reaction.

The velocity of reduction of the nitro group, as shown in numerous examples, is higher than the velocity of chlorine removal; hence the velocity of formation of the arylhydroxylamine must be higher than that of substitution of the chlorine atom by hydrogen. Consequently, during the first phase of the cathodic process 2-chloromethyl-4-tolylhydroxylamine must be formed; if its further reduction is retarded, then it undergoes rearrangement to the corresponding chloro-substituted quinolimine.

In the experimental conditions the formation of the primary amine does not proceed strictly in the sequence represented by the above formulas. In order to clarify the course of the process we performed analyses of the electrolyte for its content of primary and secondary amino groups and obtained the results plotted in the diagram.

Up to the maxima the plots in the diagram correspond to both NHOH- and NH_2 groups. The inflection point corresponds to the completion of formation of hydroxylamine, and the remainder of the plot corresponds to the transformation of--NHOH--into $-NH_2$ and is naturally a straight line. The inflection point lies between 11.5 and 13.5 A/hours: after this period analysis reveals the formation of 0.0460-0.0506 g-equiv. of compound containing NHOH- and NH_2- groups against the calculated amount of 0.0539 g-equiv., i.e., 85-93%. In these conditions, however, the yield in the form of xylidine is only 30.1% of the theoretical. Consequently the reaction of formation of the hydroxylamine is accompanied by its further reduction. At the same time a portion of the hydroxylamine undergoes the above-mentioned rearrangement. The absence of a second inflection point in the experimental conditions shows that the first stage of the reaction—formation of the nitroso compound - also proceeds side by side with the reduction of the NO group to NHOH and not strictly subsequent to it. Hence the process of electrolytic reduction of the nitro group of 2-chloromethyl-4-nitrotoluene at a lead cathode simultaneously involves the three stages of the reaction of acidic reduction.



Dependence of the formation of amino and hydroxylamino derivatives on the applied current.

The character of electrolytic reduction of organic compounds is profoundly influenced by the overvoltage. Reduction of aromatic nitro compounds at a platinum or nickel cathode readily proceeds to the hydroxylamine stage. The second stage of acid reduction - to the amine - proceeds with difficulty at these cathodes. Reduction of 2-chloromethyl-4-nitrotoluene to xylidine also proceeds unsatisfactorily at cathodes, such as Ni, with a low overvoltage, whereas good results are obtained at cathodes with a high overvoltage (Zn, Pb). However, unlike aromatic nitro compounds not containing haloalkyl substituents, 2-chloromethyl-4-nitrotoluene reduces unsatisfactorily to xylidine at certain cathodes with a high (Hg) and a medium (Cu) overvoltage, while the results are still less satisfactory at certain cathodes with a high overvoltage (Sn). We know that tin deposited in a finely divided state on the surface of a cathode of another metal increases the yield of primary aromatic amines. This effect, as we have shown, is not manifested in the case of halogen-substituted aromatic nitro compounds when tin is deposited on a lead cathode. Replacement of ethyl alcohol by methyl alcohol leads to a serious drop in yield also at cathodes with a high overvoltage (Zn and, in particular, Pb), which illustrates the great influence of the medium on the electrolytic process.

Hence the character of the electrolytic reduction of halogen-substituted aromatic nitro compounds depends not only on the overvoltage which is associated with supplementary polarization of the cathode, but also on the catalytic action of the metal cathode. The most active catalyst is zinc; leads exhibit a less intense catalytic action; tin is completely devoid of catalytic activity.

EXPERIMENTAL

Electrolytic reduction of 2-chloromethyl-4-nitrotoluene. The apparatus consisted of a 2-liter glass beaker containing a porous glass diaphragm 84 mm in diameter and 180 mm high with a glass thickness of 4 mm. In the anodic space between the porous and the glass beakers a cylindrical lead anode was located. The anolyte was 10% sulfuric acid. In the cathode space inside the porous beaker was located a cathode made of various metals in the form of a perforated cylinder or spiral tube, a glass coil for cooling, a glass mechanical stirrer and a thermometer. The catholyte was a suspension of 2-chloromethyl-4-nitrotoluene in an aqueous or aqueous-alcoholic medium (1:30), containing 6.3 g sulfuric acid in 100 ml (1.3 N) or a suspension in aqueous acetic acid. The starting material for the investigation was 2-chloromethyl-4-nitrotoluene with the following characteristics:

M.p. 52-55°; Cl (hydrolyzable) 19.42%, Cl (inorganic) 0.82%; NO_2 21.66%; water 1.0%. $C_8H_8O_2NCl$. Calculated %: Cl (hydrolyzable) 19.11; content of 2-chloromethyl-4-nitrotoluene,%: from Cl content 101.4; from NO_2 content 87.1.

The amount of 2,6-bis-chloromethyl-4-nitrotoluene in crude 2-chloromethyl-4- nitrotoluene was determined by the following method: 50 g pulverized 2-chloromethyl-4-nitrotoluene was dissolved in 200 ml methyl alcohol at 35-40°, the solution was filtered from turbidity and left till the next day at room temperature. 6.1 g crystals came down with m.p. 139-144°; these were fairly pure 2,6-bis-chloromethyl-4-nitrotoluene. % content of 2,6-bis-chloromethyl-4-nitrotoluene: from Cl content 94.4; from NO_2 content 98.1.

It therefore follows that the starting material contains 87.8% 2-chloromethyl-4-nitrotoluene. All the yields calculated below were based on this assumption.

Electrolytic reduction proceeds according to the equation:

$$ClCH_2C_7H_6NO_2 + 8H^+ + 8e \rightarrow C_8H_9NH_2 + 2H_2O + HCl,$$

and consequently the reduction of 1 mole 2-chloromethyl-4-nitrotoluene will consume $25.86 \times 8 \rightleftharpoons 215$ A/hours.

With progressive electrolytic reduction in the alcoholic electrolyte, the suspension of 2-chloromethyl-4-nitrotoluene gradually went into solution. At the conclusion of the electrolysis the nearly transparent solution was filtered (the residue was mainly the more difficultly soluble 2,6-bis,chloromethyl-4-nitrotoluene); the solvent was distilled off, toward the end with steam. The aqueous residue was treated with 10% sodium hydroxide until a permanent red color was imparted to phenolphthalein paper, after which the separated o-4-xylidine was distilled off with steam. Ammonia was detected during the initial distillation. The aqueous distillate was cooled, and after separation of the crystalline product the liquor was again steam-distilled. o-4-Xylidine was obtained in the form of faint yellow crystals analyzing (nitrite method) at 95.5, 96.7, 94.1, 95.5, 98.1% or an average of 96%. After purification by vacuum distillation, the product melted at 48-49°.

Found %: N 11.68 (Kjeldahl), $C_8H_{11}N$. Calculated %: N 11.57.

Influence of the medium (solvent) on the electrolytic reduction. The effect of various solvents on the xylidine yield was studied in a series of reductions of 2-chloromethyl-4-nitrotoluene at a Pb cathode with a current density of D 2.5A/dm², a temperature of 28-30°, a current consumption of 25 A-hours (110% excess over the theoretical); electrolysis was effected at a voltage of 5-6 V. 10 g of 2-chloromethyl-4-nitrotoluene was used in each experiment. The suspension of 2-chloromethyl-4-nitrotoluene did not go into solution completely when using a catholyte of methyl alcohol, acetic acid or water. The experimental results are presented in Table 1.

The fall in yield of xylidine in dilute alcohol solutions and even more so in water is the natural consequence of the decreasing solubility of 2-chloromethyl-4-nitrotoluene. Electrolytic reduction also takes place in acetic acid but the xylidine yield is quite unsatisfactory. The drop in yield when using methyl alcohol is noteworthy.

TABLE 1

Expt. No.	Solvent	Yield of xylidine (%)
60	75% ethyl alcohol	72.0
63	30% ethyl alcohol	21.8
39	75% methyl alcohol	46.9
73	75% acetic acid	26.8
62	Water	5.0

TABLE 2

Expt. No.	Temp.	Yield of xylidine (%)
4	10°	8.4
56	21	68.6
60	30	72.0
85	30	72.0
47	38	72.0
7	42	67.0
7°	45	58.6

TABLE 3

Expt. No.	D, A/dm²	Yield of xylidine (%)	Expt. No.	D, A/dm²	Yield of xylidine (%)
21	1.0	62.3	54	2.5	69.6
28	2.0	67.0	46	4.5	72.0
32	2.5	70.4	69	6.0	64.0
60	2.5	72.0	25	8.0	57.0
85	2.5	72.0	75	10.0	45.2

Effect of temperature. The temperature effect was studied at between 10 and 45°. Experiments were performed in an electrolyzer with a Pb cathode in 75% ethyl alcohol in presence of sulfuric acid; D = 2.5 A/dm²; A-hours 25-30; weight of starting substance 10 g.

The results (Table 2) show that within the temperature range of 30 to 40° a change of temperature does not affect the yield. Higher temperatures reduce the yields and lower temperatures do so even more markedly.

TABLE 4

A-hours	11.5	15	25
No. of expt.	98	48	60
Yield of xylidine (%)	31.7	45.3	72.0
Current yield (Y%)	29.3	32.0	30.0

TABLE 5

Expt. No.	A/dm²	Xylidine yield (% of theory) in dependence on the cathode material (in ethyl alcohol)						
		Zn	Pb	Sn on Pb	Hg	Cu	Ni	Sn
24	2.5	78.7	–	–	–	–	–	–
60	2.5	–	72.0	–	–	–	–	–
85	2.5	–	72.0	–	–	–	–	–
92	2.5	–	70.4	–	–	–	–	–
32	2.5	–	70.4	–	–	–	–	–
57	2.5	–	–	62.8	–	–	–	–
58	2.5	–	–	58.9	–	–	–	–
15	2.5	–	–	–	52.0	–	–	–
16	2.5	–	–	–	52.5	–	–	–
88	2.5	–	–	–	–	45.2	–	–
87	6.0	–	–	–	–	–	20.1	–
8	2.5	–	–	–	–	–	–	10.0

Current density. The effect of change of current density on the reduction of 2-chloromethyl-4-nitrotoluene was studied over the range of 1 to 8 A/dm². The same apparatus as before was used in the same conditions except for the variation of current density (Table 3).

We see from Table 3 that the yield is not affected by a change in current density between 2 and 4.5 A/dm². A marked drop in yield follows the raising of the current density to 8 A/dm² or its fall to 1 A/dm².

Current yield. In our investigation of the effect of various factors on the electrolytic reduction of 2-chloromethyl-4-nitrotoluene we calculated the yield on the basis of the amount of substance formed with an amount of current sufficient for definite completion of the process. It is also of interest to determine the current yield of xylidine (Y%), as defined by the formula:

$$Y\% = \frac{M \cdot 100}{0.562 \cdot Q},$$

where M is the weight of xylidine formed; 0.562 is the theoretical amount of xylidine formed under the action of 1 A/hour; Q is the amount of consumed electricity (in A-hours).

Experiments were performed in 75% ethyl alcohol with the usual ratios of reagents at 30° (Table 4).

Complete reduction of 2-chloromethyl-4-nitrotoluene theoretically requires 11.5 A-hours.

Dependence of the electrolytic reduction on the cathode material. Cathodes of Hg, Pb, Zn, Sn, Cu and Ni were employed. Experiments were performed in 75% ethyl alcohol in presence of sulfuric acid at 28–30°; weight of starting material 10 g. Results are presented in Table 5.

TABLE 6

Expt. No.	A/dm^2	Xylidine yield (% of theory) in dependence on the cathode material (in methyl alcohol)					
		Zn	Pb	Hg	Cu	Ni	Sn
66	2.5	68.6	–	–	–	–	–
39	2.5	–	46.9	–	–	–	–
67	2.5	–	–	46.8	–	–	–
17	2.5	–	–	–	45.3	–	–
68	2.5	–	–	–	–	16.7	–
65	2.5	–	–	–	–	–	11.7

TABLE 7

Expt. No.	% Content of suspension	D A/dm^2	Xylidine yield (%)
54	3.3	2.5	69.6
85	3.3	2.5	72.0
26	6.6	4.0	74.0

TABLE 8

Expt. No.	Current passed, A-hours from start of expt.	NHOH and NH$_2$ content of solution calculated on the xylidine (in %)	Total content of NHOH and NH$_2$ groups calculated on xylidine (in g)
44	2.5	0.58	1.88
	5.0	1.02	3.44
	7.5	1.32	4.05
	10.0	1.60	4.96
	12.5	1.83	5.58
	15.0	1.86	5.58
	17.5	1.86	5.48
	20.0	1.86	5.39
46	5.0	1.08	3.34
	9.0	1.47	4.48
	13.0	1.77	5.31
	17.5	1.83	5.39
	21.5	1.80	5.22
98	2.5	0.45	1.44
	5.0	0.75	2.36
	10.0	1.25	3.78
	11.5	1.40	4.20

The series of metals – Sn, Ni, Cu, Hg, Pb, Zn – arranged in order of increasing yield of xylidine has a different order from that of the metals in the overvoltage series. Slightly different results are obtained when the electrolysis is carried out in methyl alcohol. The order of the metals, when arranged in accordance with increasing yields of xylidine, remains the same, but the yield is strongly reduced at the zinc and, in particular, at the lead cathode (Table 6).

Effect of concentration of substance on yield. Several experiments were performed at a lead cathode in 75% ethyl alcohol in presence of sulfuric acid (Table 7).

When the catholyte contains 3.3-6.6% starting material, the yield of xylidine is seen to be almost constant.

Formation of primary and secondary amino groups during the reaction. The proportions of primary and secondary amino groups formed during electrolysis were determined by the following procedure: 5 ml electrolyte was filtered from the precipitate and titrated in a strongly acid medium (while cooling) with 0.05 N sodium nitrite solution. The analytical results of three experiments are detailed in Table 8 and plotted in the diagram. 10 g starting material was used in each experiment.

In conclusion we express our gratitude to V. A. Devyatina and L. N. Kravchina for performing the analyses.

SUMMARY

1. A study was made of the dependence of the electrolytic reduction of halo-alkyl-substituted aromatic nitro compounds on the cathode material, the medium, the temperature, the current density and other factors.

2. It was shown that the electrolytic reduction of 2-chloromethyl-4-nitrotoluene proceeds with increasing yields of the xylidine in the following order of cathode materials: Sn, Ni, Cu, Hg, Pb, Zn.

3. The difference between this order and the order of the metals in the overvoltage series is explained by the catalytic action of the cathode material.

4. The most active catalyst for the electrolytic reduction of haloalkyl-substituted aromatic nitro compounds is zinc; next in order is lead; complete absence of catalytic action is found with tin.

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THE MECHANISM OF THE REACTION OF CHLOROSULFONIC ACID WITH SOME AROMATIC COMPOUNDS

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The problem of the mechanism of reaction of chlorosulfonic acid with aromatic compounds had not been closely studied up to now and has remained controversial. Thus in a monograph on the sulfonation of organic compounds, I. S. Ioffe [1] bluntly states that "...up to now the course of the reaction of chlorosulfonic acid with sulfonatable substances is unclarified". The theory is extremely widespread that the first products of the reaction are sulfochlorides:

$$ArH + ClSO_3H \longrightarrow ArSO_2Cl + H_2O. \qquad (1)$$

The released water decomposes the excess of chlorosulfonic acid into hydrogen chloride and sulfuric acid; the latter sulfonates the organic compound to give sulfonic acids as by-products. Consequently the presence of sulfonic acids is regarded as the result of a secondary sulfonation reaction with sulfuric acid [2,3,4,5]. This theory does not appear to have been experimentally confirmed at any time; as will be shown below, it does not reflect the actual course of the reaction with sufficient completeness and accuracy.

Experimental studies with various compounds – toluene [6], naphthalene [7] and acetanilide – have shown that for these compounds the reaction is more correctly represented on the basis of initial formation of sulfonic acids by the action of chlorosulfonic acid:

$$Ar\boxed{H + Cl}SO_3H \longrightarrow ArSO_3H + HCl. \qquad (2)$$

Subsequently the sulfonic acids are transformed into sulfochlorides according to the scheme:

$$ArSO_2\boxed{OH + HSO_3}Cl \longrightarrow ArSO_2Cl + H_2SO_4. \qquad (3)$$

According to this mechanism sulfonic acids are mainly formed as the result of incompleteness of the chlorosulfonation reaction.

Clarification of the true mechanism of the reactions is very necessary for a realistic and efficient operation of the industrial processes for sulfochlorides, since the first theory indicates that the process should be interrupted at the earliest possible moment to give a maximum yield of sulfonic acids, while the second theory requires that the process should be prolonged until the maximum amount of sulfonic acids has been converted into sulfochlorides. The clarification of the mechanism of this complex reaction, which includes a series of parallel and consecutive processes, is greatly complicated by the formation, sometimes in high yields, side by side with sulfonic acids and sulfochlorides, of sulfones, polysulfonated derivatives, chloro derivatives, side chain-substituted oxidation products and many other substances which undergo reciprocal transformations.

For the purpose of arriving at a preliminary solution of the main problem – the mechanism of the entry of the chlorosulfonic group into an organic molecule – we carried out some thermodynamic calculations. The changes of free energy and of entropy of the individual reactions were calculated for a series of aromatic compounds.

For the purpose of gaining insight into the mechanism of a reaction it is important to know not only the direction of the reaction and the degree of conversion – which are governed by the sign and magnitude of the free energy – but also the velocity of the individual reaction steps. The reaction velocity is governed, according to modern concepts, by the probability of formation of an active complex; in this connection the probability factor P appears to be related to the entropy of activation ΔS^* by the expression:

$$PZ = e^{\frac{\Delta S^*}{R}} \cdot \frac{kT}{h},$$

insofar as the theoretical number of collisions (Z), Boltzmann's constant (k), the gas constant (R) and Planck's constant (h) are substantially constant at the given temperature (T).

The lack of knowledge at the present time of the properties of the active complex is a serious hindrance to the calculation of the entropy of its formation. But since the active state exists between the commencing and final states, we can draw certain qualitative conclusions from a consideration of the total change of the entropy process ΔS.

We know that by using ΔS in place of ΔS^{*} for the evaluation of reaction velocity it is possible to arrive at serious deviations in the quantitative expression of the probability factor P, which plays an important part in the kinetic equation:

$$K_V = PZe^{\frac{-E}{RT}},$$

where K_V is the velocity constant and E is the activation energy.

However, for homogeneous reactions with structurally similar compounds existing in very similar states, a qualitative, roughly orientating, comparative evaluation of the reaction velocity with the help of ΔS, can be performed with a measure of accuracy. Thus, if in the case of one of two heterogeneous reactions ΔS has a high positive value, then we must expect that the given reaction will be faster, while if the value is more negative then the reaction should be slower [17].

In other cases an evaluation of reaction velocity on the basis of ΔS will be less accurate. Nevertheless a comparison of the change of entropy of two similar reactions, especially when they differ not only in magnitude but also in sign, permits an evaluation of the degree of probability of the arbitrary occurrence of each of them in an isolated system, the probability being related in a definite manner to the velocity of the process.

We defined the entropy of a process at 25°C as the difference between the entropies of formation of the reaction products and the starting substances. The entropy of formation of all the compounds was calculated as the difference between the standard entropy of the compound and the standard entropy of the elements entering into it.

The entropy of the elements was taken from the data of Parks and Huffman [9] and the entropy of the compounds was calculated from the formulas of I. I. Strelkov [10].

TABLE 1

Calculated Values of Entropy Changes (ΔS in electrostatic units), Heats (ΔH in kcal) and Free Energy (ΔF in kcal) for Reactions of the Type:

A) $X{-}C_6H_5 + ClSO_3H \longrightarrow X{-}C_6H_4{-}SO_3H + HCl$;
B) $X{-}C_6H_5 + ClSO_3H \longrightarrow X{-}C_6H_4{-}SO_2Cl + H_2O$;
C) $X{-}C_6H_4{-}SO_3H + ClSO_3H \longrightarrow X{-}C_6H_4{-}SO_2Cl + H_2SO_4$.

X	Name of compound	A			B			C		
		ΔS	ΔH	ΔF	ΔS	ΔH	ΔF	ΔS	ΔH	ΔF
$-H$	Benzene	0	−31.4	−31.4	+ 1.0	−21.3	−21.0	+10.7	+ 4.1	+ 0.9
$-CH_3$	Toluene	− 2.6	−42.8	−42.0	−31.0	−36.0	−26.7	−19.0	+ 0.7	+ 6.6
$-NH_2$	Aniline	+ 1.2	−34.8	−35.2	−24.7	−26.8	−19.5	−13.8	+ 1.9	+ 6.0
$-NH\frac{CO}{2}$	Carbanilide	+24.5	−47.5	−54.8	+22.7	−41.4	−48.2	+17.2	−18.9	−24.0
$-NHCOCH_3$ . .	Acetanilide	+13.2	−32.3	−36.9	−13.1	−22.7	−19.1	−15.7	+ 3.9	+ 8.6
$-NHCOH$ . . .	Formanilide	+12.8	−61.8	−65.1	−13.2	−28.9	−24.3	−15.6	+26.7	+31.3

The solid substances at 298°K:

$$S_{298^\circ} = 2.0\,(C) + 2.5\,(H + N) + 4.4\,(O) + 10.0\,(Cl + Br + I) + 7.0\,(m).$$

For liquids at the same temperature:

$$S_{298^\circ} = 3.5\,(C) + 3.2\,(H) + 9.1\,(O) + 11.9\,(Cl + Br + I) + 9.8\,(N).$$

In these formulas C, H, N, O, Cl, Br, and I signify the number of atoms of the respective elements in a molecule, and m is the total number of other atoms.

The change of free energy of a process at 25°C was defined as the difference between the standard free energies of the products and the starting substances.

The free energy of the products ($\Delta F_{prod.}$) and the starting components ($\Delta F_{init. subs.}$) are calculated from the equation:

$$\Delta F_{298°} = \Delta H - T\Delta S_{298°}.$$

The heats of formation of the compounds from the elements $-\Delta H-$ were taken either from the literature or calculated from the equation:

$$\Delta H = H_{comb.} - [94.38\,(C) + 34.19\,(H) + 0(Br + Cl + I + N + O) + 41.4F + 69.3S].$$

In the case of absence from the literature of data for the heats of combustion ($H_{comb.}$) these were calculated from the Kharasch formula with corrections for the heat of fusion of solids.

Some of our calculated data are set out in Table 1.

It follows from consideration of these data that in the reaction of chlorosulfonic acid with aromatic compounds the formation of sulfonic acids and sulfochlorides is equally possible since the change of free energy of these processes has a large negative value. A comparison of the magnitudes of the change of entropy indicates, however, that the degree of probability of these processes is likely to vary with different compounds.

The probability of type A reactions for toluene, aniline, acetanilide and formanilide must be considerably higher than the probability of type B reactions, because in the first case the increase of ΔS is greater. This signifies that side by side with the direct formation of sulfochlorides proceeding at low velocity, the main mass must evidently be formed from sulfonic acids according to scheme (C) since the formation of the latter in scheme (A) must proceed with a higher velocity and with a higher yield.

In the case of carbanilide the entropy change of reactions (B) and (A) are substantially identical. It may be assumed that the formation of sulfonic acids as well as the direct formation of sulfochlorides must take place with similar velocities. Since, however, sulfonic acid formation involves a bigger drop in free energy, it will take place with a somewhat higher yield.

Formation of benzene sulfochloride according to schemes (A) and (B) also appears to have equal probability, although the first process must give a slightly higher yield. Benzene sulfochloride appears to be formed with similar velocities by both schemes. Formation of sulfochlorides according to scheme (C) at 25°C from toluene, acetanilide and formanilide will be hindered and will require a supply of heat from outside. In these conditions benzene sulfonic acid and the sulfonic acid of carbanilide must undergo ready transformation into sulfochlorides. These assumptions find confirmation in practical operation of the processes. Whereas the preparation of the sulfochlorides of toluene, acetanilide and formanilide can be effected either by reaction over a prolonged period or at a temperature of 60-80°, benzene sulfonic acid is obtained in good yield by reaction for a short period at 20-25°.

Thus the thermodynamic calculations show that in chlorosulfonation reactions formation must take place simultaneously of both sulfonic acids and (directly) of sulfochlorides. The degree of probability of these reactions depends on the type of starting compound and on the reaction conditions. It is consequently impossible to single out any one of the above schemes as corresponding to the mechanism of chlorosulfonation. In other words none of these schemes can be regarded as a general scheme of chlorosulfonation, since it is always necessary to specify the type of compound used and the reaction conditions.

For the purpose of experimental verification of the conclusions reached from thermodynamic calculations, we performed a series of experiments on the influence of temperature, duration of reaction and ratios of components on the yields of sulfochlorides and sulfonic acids during chlorosulfonation of various aromatic compounds.* Most of the experiments were performed by the following procedure:

With energetic stirring the organic compound was gradually added to the calculated amount of chlorosulfonic acid at a definite temperature which was maintained with the help of a thermostat. The resultant reaction mass was then held for a definite period at the specified temperature. The reaction was terminated and the product isolated by pouring the mass into a large volume of water at the given temperature under vigorous stirring. The products were liquids or solids and were separated from the aqueous solution, washed with distilled water until all traces of sulfuric and hydrochloric acids had been removed, dried to constant weight, and analyzed. The aqueous solution of organic substances and inorganic acids together with the wash waters was also analyzed. The organic compounds were sometimes isolated from this solution. For this purpose the solution was neutralized with ammonia solution or 10% sodium hydroxide and evaporated to dryness, and the dry residue extracted in a Soxhlet with alcohol, acetone or other common solvent for removal of the organic compound.

TABLE 2

Yields of Sulfochlorides, Sulfonic Acids and Sulfones in the Chlorosulfonation of Aromatic Compounds over a Period of 2 Hours.

Expt. No.	Compound	Molar ratio of compound to chlorosulfonic acid	Temp. (°C)	Yields (mole-%)			
				of unreacted compound	of sulfochlorides	of sulfonic acids	of sulfones
1	Benzene	1:1	–40	46.5	Traces	53.2	Traces
2	"	1:1	25	–	7.8	89.2	3.0
3	"	1:1	90	–	12.0	80.2	7.7
4	"	2:1	25	–	4.9	–	4.3
5	Toluene	1:1	–40	63.5	Traces	35.2	–
6	"	1:1	25	–	4.6	87.2	4.5
7	"	1:1	90	–	10.3	*	9.7
8	o-Xylene	1:1	25	–	2.0	93.2	–
9	Naphthalene	1:1	25	–	3.2	94.6	–
10	Acetanilide	1:1	25	–	2.5	96.9	–
11	"	1:5	25	–	9.6	89.8	–
12	"	1:5	60	–	82.4	*	–
13	Carbanilide	1:1	25	–	9.2	*	–
14	"	1:5	25	–	28.2	*	–
15	"	1:5	60	–	65.3	*	–
16	Formanilide	1:1	25	–	2.5	98.0	–
17	"	1:5	25	–	11.0	88.3	–
18	"	1:5	60	–	75.2	*	–
19	Phenol	1:1	25	–	Traces	96.8	2.5
20	Nitrobenzene	1:1	25	–	1.8	94.2	2.7

The sulfochlorides were identified from their melting or solidifying points after purification (by vacuum distillation or recrystallization from benzene, acetone or dichloroethane). The sulfonic acids were identified by the melting points of their chlorides, which were obtained by treatment of the sodium salts with phosphorus pentachloride; sometimes they were identified through the amides, prepared by the action of aqueous ammonia or ammonium carbonate on the sulfochlorides. For evaluation of the general course of the reaction (sulfonation, chlorination or chlorosulfonation), a sample of the reaction mass was analyzed for its content of organically bound sulfur and chlorine.

The experimental data (Table 2) show that sulfonic acids are the main products in the reaction of equimolar amounts of chlorosulfonic acid with aromatic compounds, the amount of sulfochlorides not usually exceeding 10% of theory. The amount of sulfonic acids considerably exceeds the amount of sulfochlorides in the first instant of reaction also when using large excesses of chlorosulfonic acid, particularly at low temperature.

The formation of a large amount of sulfonic acids in the first stage of the reaction may be explained both by the sulfonating action of chlorosulfonic acid and by the presence of sulfuric acid also formed by hydrolysis of chlorosulfonic acid by the water released in accordance with equation (1).

It can be shown with the help of thermodynamic calculations that sulfonation with chlorosulfonic acid must take place much more readily than sulfonation with sulfuric acid. In fact, applying Hess's law we see that the difference between changes of entropy, free energy and thermal effects for sulfonation of any organic compound according to the schemes:

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* Yields of sulfonic acids not specified since mixtures of sulfonic acids with different degrees of sulfonation are formed.

$$ArH + ClSO_3H \longrightarrow ArSO_3H + HCl \text{ and } ArH + H_2SO_4 \longrightarrow ArSO_3H + H_2O,$$

can be numerically expressed by the change of these magnitudes for the process:

$$ClSO_3H + H_2O \longrightarrow H_2SO_4 + HCl.$$

For this process our calculations give a value for ΔS of approximately +10.46 electrostatic units, and for ΔF of about −20.430 cal.

Sulfonation with chlorosulfonic acid must consequently proceed more rapidly and with a higher yield of products than sulfonation with sulfuric acid.

These considerations are confirmed in practice. Thus, benzene [11], toluene [6,12] and acetanilide [13] are sulfonated by chlorosulfonic acid more rapidly and at a lower temperature; anthrone [14] does not form sulfonic acids under the action of sulfuric acid at 180° but is sulfonated by chlorosulfonic acid even at 60-70°.

In the light of the above facts it must be stated that, notwithstanding the opinions of many authors [2,3,4,5], the secondary reaction with sulfuric acid during the process of chlorosulfonation can scarcely play an essential part and recedes even further into the background at high concentrations of chlorosulfonic acid, particularly at the start of the process. The main mass of sulfonic acids formed by the process consists of products of reaction with chlorosulfonic acid [equation (2)] and not with sulfuric acid.

In the second stage of the process the sulfonic acids undergo conversion into sulfochlorides in accordance with equation (3). This reaction takes place slowly and in the majority of cases it requires energy from outside.

In Figure 1 is plotted the change in amount of organic sulfur (curves S) and organic chlorine (curves Cl) in course of time during the process of chlorosulfonation of acetanilide at 25 and 40°. We see from the curves that the amount of organic sulfur reaches a value of nearly 100% (calculated on the monosulfo derivative) almost immediately after completion of the make-up of the batch (i.e. within 15 minutes); it then remains nearly constant throughout the whole process. On the other hand the amount of organic chlorine and the corresponding amount of separated sulfochloride (curve CX) are respectively 10 and 20% after make-up and gradually rise to a maximum before slowly falling. Curve CK, representing the change in amount of sulfonic acid in the reaction mass, and curve CX form an almost symmetrical pair, which fact confirms the reciprocal transitions: sulfonic acid ⇄ sulfochloride. At temperatures above 40° in the case of acetanilide this symmetry is upset due to reactions of di- and trisulfonation.

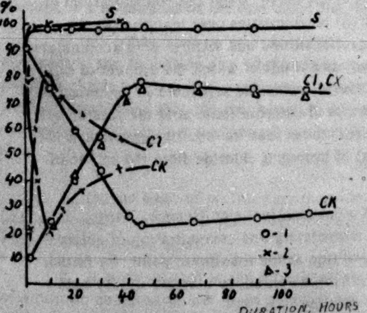


Fig. 1. Accumulation of organic sulfur (S) (in % of the theoretical for the monosulfochloride); organic chlorine (Cl) (in % of the theoretical for the monosulfochloride); yields of sulfochloride (CX) and of sulfonic acid (CK)(in % of the theoretical for chlorosulfonation of acetanilide). 1) at 25°; 2) at 40°; 3) sulfochloride at 25°.

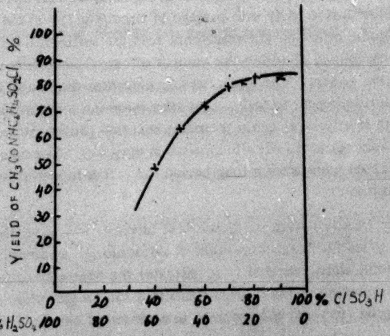


Fig. 2. Dependence of the yield of p-acetaminobenzene sulfochloride (in % of theory based on the composition of the inorganic portion of the reaction mass) at the conclusion of the process at 60°C in states close to equilibrium.

The course of curve Cl in Fig. 1 is characteristic of the chlorosulfonation of aromatic compounds in representing the kinetics of the slowest stage – the stage of transition of the sulfonic acid into the sulfochloride (equation 3).

It is reported in the literature [15] that at a temperature of about 100°, toluene sulfochloride is decomposed by sulfuric acid with formation of toluene sulfonic acid and evolution of hydrogen chloride and sulfur trioxide. We tested the possibility of effecting this reaction with various sulfochlorides at various temperatures. We established the general character of this reaction also at low temperatures (–40 and –20°C), when it may proceed with formation of chlorosulfonic acid:

$$ArSO_2Cl + H_2SO_4 \longrightarrow ArSO_3H + ClSO_3H.$$

Hence the reaction of formation of sulfochloride from sulfonic acid may be regarded as a reversible one. At normal and high temperatures it proceeds irreversibly due to dissociation of chlorosulfonic acid, which is caused by the influence of the large amount of heat released in the transition from sulfochloride to sulfonic acid:

$$ClSO_3H + 14.9_{cal.} \rightleftharpoons HCl + SO_3,$$

and the process can be essentially represented by the scheme:

$$ArSO_2Cl + H_2SO_4 \longrightarrow ArSO_3H + HCl + SO_3. \qquad (4)$$

An equilibrium is established between the concentrations of the products of reactions (3) and (4), which depends on the ratios of the velocities of these reactions at the given temperature. Due to this, in each such system it is only possible to obtain a certain yield of sulfochloride when the state of the system is close to equilibrium. Consequently the yield of sulfochloride depends, apart from the nature of the organic compound, the temperature and the duration of the process, on the composition of the reaction mass at the conclusion of the process, and, in particular, on the concentrations of chlorosulfonic and sulfuric acids; the latter, in turn, depend on the excess of chlorosulfonic acid used in the reaction and its concentration. This dependence is illustrated in Figure 2 for acetaminobenzene sulfochloride in states close to the equilibrium state.

Specially performed experiments showed that when the composition of the inorganic portion of the reaction mass at the conclusion of the process was 65% chlorosulfonic acid and 35% sulfuric acid, the molar ratio of benzene sulfonic acid to benzene sulfochloride at 25° was 0.3:0.7 irrespective of whether we started from benzene sulfonic acid and chlorosulfonic acid or from benzene sulfochloride and the calculated amount of a mixture of sulfuric and chlorosulfonic acids.

On the basis of the foregoing facts we can understand the course of the curve of change of amount of sulfochloride (CX) with passage of time (Fig. 1). In the rising branch of the curve, when the concentrations of sulfonic acid and chlorosulfonic acid are sufficiently high, reaction (3) predominates over reaction (4), in consequence of which the amount of organic chlorine increases and sulfochloride and sulfuric acid accumulate in the system. This progressively promotes the course of reaction (4), as a result of which the amount of sulfochloride begins to fall slowly after reaching a certain magnitude. The sulfochloride separated in accordance with reaction (4) again promotes reaction (3); hence with a large excess of chlorosulfonic acid the rate of fall of concentration of sulfochloride is very low. The course of curves (Cl) shows that the equilibrium state is not attained even after a long period, as it is hindered by the removal of hydrogen chloride from the sphere of reaction.

Apart from its theoretical interest, the curve in question has great practical significance. First it specifies the maximum yield of sulfochloride attainable at a given temperature and concentration of chlorosulfonic acid. Second, it indicates the necessity to interrupt the reaction at the maximum point, for further continuation of the process leads to a fall in the sulfochloride yield. This statement refutes the widely held opinion [16] that the reaction mass does not change after prolonged standing.

The above facts also compel us to reject the conclusion of L. S. Solodar [13] to the effect that sulfuric acid does not play a decisive part in the process of chlorosulfonation. Sulfuric acid plays an important part since, by lowering the concentration of chlorosulfonic acid and reacting with the resultant sulfochlorides, it must govern the yield of the latter.

It follows from curve (Cl) in Figure 1 that whereas the amount of chlorine increases relatively slowly, at the starting point immediately after addition of the organic compound (which takes a period of 15 minutes) it has a value of about 10% of the theoretical. From this we must conclude that the presence of such a high percentage cannot be due to the transformation of sulfonic acid into sulfochloride [reaction (3)]. It is clear that for the greater part it could only have been formed at the expense of direct introduction of the SO_2Cl-group into the organic molecule by reaction with chlorosulfonic acid during the first stage of the reaction in accordance with equation (1); this is consistent with our preliminary conclusions reached on the basis of thermodynamic calculations.

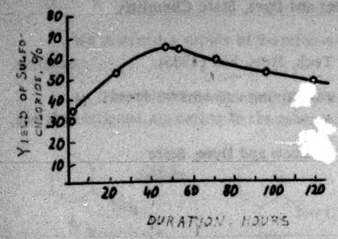
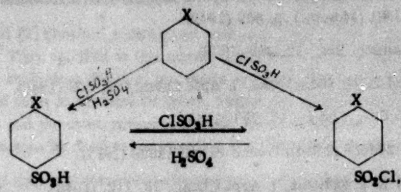


Fig. 3. Dependence of the yield of p,p'-disulfochloride of carbanilide on time during reaction at 25°

According to these calculations (Table 1), reaction (1) for carbanilide at 25°C must proceed with a velocity much closer to that of reaction (2) than is the case for acetanilide. Experiment confirms this conclusion. Whereas the mean velocity of accumulation of chlorine in the reaction mass after the completion of the addition of material is 1.08% of the theoretical amount in an hour (Fig. 3), the amount of chlorine immediately after the addition (over a period of one half hour) was 30% of theory, reckoned on one SO_2Cl group per benzene ring.

On the basis of thermodynamic calculations and experimental data we may propose the following simplified scheme as being most probable for the reaction of chlorosulfonic acid with aromatic compounds:



where X is a substituent of the first order and the dense arrow indicates the preferred direction of reaction.

In this connection we must not forget that the true course of the reaction is considerably more complex and leads to the formation of a whole series of products: sulfones, polysulfo derivatives, chloro derivatives, products of side-chain substitution, etc. In the case, for example, of the reaction with aromatic acylamines, we have established that the first reaction products are acylsulfamino acids and their chlorides, which subsequently change into nuclear-substituted acylamines.

SUMMARY

1. On the basis of preliminary thermodynamic calculations and of experimental investigations a scheme has been established for the main reactions during chlorosulfonation of aromatic compounds with formation of chlorides of sulfonic acids.

2. It is shown that in the first rapid stage of the reaction between chlorosulfonic acid and the majority of aromatic compounds, the main products are sulfonic acids, while sulfochlorides are obtained in minor amounts. Sulfonation with sulfuric acid, when using high concentration of chlorosulfonic acid, does not play an important part.

3. In the second, slow, stage of the process the sulfonic acids are transformed into sulfochlorides under the action of excess of chlorosulfonic acid, and sulfuric acid is released. The reaction may be reversible at low temperatures and proceeds irreversibly at elevated temperatures due to breakdown of the chlorosulfonic acid (released during the reversible reaction) into sulfur trioxide and hydrogen chloride, and removal of the latter from the sphere of reaction.

4. Sulfuric acid plays an important part during chlorosulfonation, lowering the concentration of chlorosulfonic acid and reacting with the sulfochlorides to convert them into sulfonic acids. Consequently its presence in the reaction mass governs the yield of sulfochlorides in the given conditions for operation of the process.

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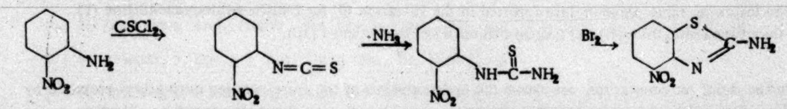
* See Consultants Bureau translation, p. 945.

THE PROBLEM OF THE THIOCYANATION OF o-NITROANILINE

S. G. Fridman

We required a supply of 2-amino-4-nitrobenzothiazole. In the literature we found three references to its synthesis.

1. The compound was prepared for the first time by Dyson, Hunter and Morris [1] from o-nitroaniline and thiophosgene according to the scheme:



They reported a m.p. of 232° for their 2-amino-4-nitrobenzothiazole.

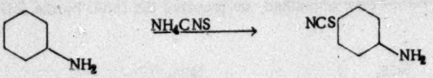
2. Erlenmeyer and Ueberwasser [2] improved the preceding method and obtained a nearly quantitative yield of 2-amino-4-nitrobenzothiazole with m.p. 254°.

3. Blomquist and Diuguid [3] obtained a compound with m.p. 110-112° by thiocyanation of o-nitroaniline by Kaufmann's method. They ascribed to this substance the structure of 2-amino-4-nitrobenzothiazole. After purification via the acetyl derivative the m.p. was raised to 130°. The acetyl derivative melted at 138-139°. Blomquist and Diuguid refer to the work of Dyson, Hunter and Morris; however the difference of 102° in the melting point of one and the same substance did not disturb them in the least. They then converted their amine into the chloro derivative by Sandmeyer's method and obtained a substance melting at 59.5-61.5°.

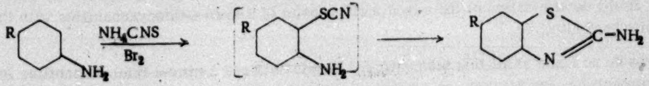
The authors assumed that they had obtained 2-chloro-4-nitrobenzothiazole, although Erlenmeyer and Ueberwasser 7 years previously had prepared 2-amino-4-nitrobenzothiazole and from it had obtained, via the diazo compound by Sandmeyer's method, 2-chloro-4-nitrobenzothiazole with m.p. 169-170°.

We were astonished not only by the discrepancy in the melting points but also because the American chemists, Blomquist and Diuguid, had applied Kaufmann's method without bothering to mention the fact.

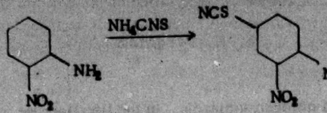
According to Kaufmann [4] and other workers [5], the first stage in the thiocyanation is the substitution of a thiocyanogen group for a hydrogen atom in the para-position to the amino group:



If the para-position is occupied, then substitution takes place in the ortho-position to the amino group and is accompanied by cyclization to a derivative of 2-aminobenzothiazole:



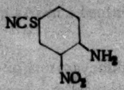
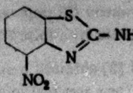
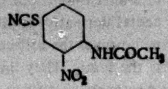
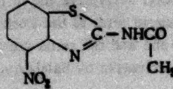
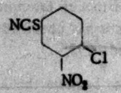
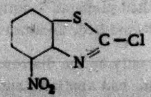
Consequently in the thiocyanation of o-nitroaniline by Blomquist and Diuguid in their specified conditions, only 2-nitro-4-thiocyanoaniline could be formed and not a derivative of 2-aminobenzothiazole.



The empirical formulas of 2-nitro-4-thiocyanoaniline and 2-amino-4-nitrobenzothiazole are identical. Hence the analytical data cannot be regarded as proof of the correctness of the authors' claims.

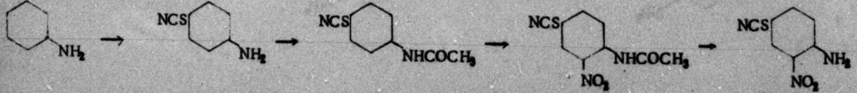
The following table presents data reported in the literature [6] for 2-nitro-4-thiocyanoaniline (I), 2-nitro-4-thiocyanoacetanilide (II) and 2-nitro-4-thiocyanochlorobenzene (III).

On the right, for comparison, are shown the melting points of the corresponding derivatives prepared by Blomquist and Diuguid by thiocyanation of o-nitroaniline and by replacing the amino group by chlorine:

Preparation	Thiocyano derivatives		Preparations of Blomquist and Diuguid	
No.	Structure	m.p.	Structure attributed by the authors	m.p.
I		113°		110-112°
II		138-139		138-139
III		63		59.5-61.5

We see from the table that the melting points of the corresponding compounds are the same or nearly so.

In order to prove that the product obtained by Blomquist and Diuguid by thiocyanation of o-nitroaniline is not 2-amino-4-nitrobenzothiazole but 2-nitro-4-thiocyanoaniline, we prepared the latter by the following scheme as given in the literature [6]:



In the conditions described by the authors we obtained from o-nitroaniline the alleged 2-amino-4-nitrobenzothiazole and its acetyl derivative. The melting point of a mixed sample of 2-nitro-4-thiocyanoacetanilide with the acetyl derivative of the alleged 2-amino-4-nitrobenzothiazole did not suffer any depression. Nor was any depression observed in the determination of the mixed melting point of 2-nitro-4-thiocyanoaniline with the alleged 2-amino-4-nitrobenzothiazole.

There can thus be no doubt at all that Blomquist and Diuguid obtained 2-nitro-4-thiocyanoaniline in the thiocyanation of o-nitroaniline, and not 2-amino-4-nitrobenzothiazole. The compound which they prepared by replacing the amino group by chlorine was 2-nitro-4-thiocyanochlorobenzene and not 2-chloro-4-nitrobenzothiazole.

SUMMARY

It is shown that Blomquist and Diuguid obtained 2-nitro-4-thiocyanoaniline by thiocyanation of o-nitroaniline, and not 2-amino-4-nitrobenzothiazole as they erroneously concluded.

They obtained 2-nitro-4-thiocyanoacetanilide on acetylation of the product, and not 2-acetamino-4-nitrobenzothiazole; by diazotization followed by treatment with cuprous chloride these authors obtained 2-nitro-4-thiocyanochlorobenzene to which they erroneously ascribed the structure of 2-chloro-4-nitrobenzothiazole.

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CHLOROMETHYLATION OF ARYL ALIPHATIC KETONES

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The introduction of the CH_2Cl group into the aromatic nucleus with the help of $CH_2O + HCl$ (the chloromethylation reaction) is one of the best established and most important reactions of organic synthesis in the aromatic series. Up to the present, however, there has been no known instance of the introduction of the CH_2Cl group into a chain even when special attempts have been made to effect such a reaction [1]. In July 1936 the successful chloromethylation of a series of aliphatic ketones was reported [2]:

$$R-CO-CH_3 + CH_2O + HCl \rightarrow R-CO-CH_2-CH_2Cl + H_2O.$$

Spurred on by this success, Fuson and McKeever [3] attempted to effect chloromethylation in the chain in a series of aliphatic-aromatic ketones. Success in this attempt would have provided a simple and accessible method of preparation of technically important vinylaryl ketones [4]. The authors did not achieve their objective: in the case of arylalkyl aliphatic-aromatic ketones chloromethylation did take place but the CH_2Cl group entered the ring and the aliphatic chain was not attacked; in the particular cases of acetophenone and propiophenone the reaction did not generally take place. It would thus appear that it is not possible to introduce the CH_2Cl group into a side chain by the chloromethylation reaction.

By using boron fluoride etherate $(C_2H_5)_2O \cdot BF_3$ as the catalyst* and monochlorodimethyl ether as the chloromethylating component, however, we have succeeded in effecting side-chain chloromethylation of acetophenone and propiophenone.

EXPERIMENTAL

1. Chloromethylation of propiophenone. Here we shall describe only one experiment; identical results were obtained in all the other experiments. In a thick-walled flask a mixture was prepared of 13.4 g (0.1 mole) propiophenone (B. p. 214-216°), 8 g monochlorodimethyl ether (b.p. 49-70°)** and 2.27 g boron fluoride etherate (b.p. 124-128°). The flask was tightly corked and heated in a water bath for 31 hours at 60-65° and for 1 hour at 80°. After cooling to room temperature, the reaction mass was poured into a separating funnel containing iced water, the water layer was separated, and the remainder was also washed with iced water until the reaction for boron was negative. The product was then dried over freshly calcined sodium sulfate and vacuum distilled.

12.93 g of material was fractionated: Fraction 1, 99-115° (6.5 mm), 6.84 g; fraction 2, 124-134° (6.5 mm), 4.20 g; residue, 1.25 g; losses, 0.64 g.

The first fraction proved to be unreacted ketone. The second fraction was a colorless liquid with a pungent odor, fuming in the air; it darkened on standing. Its properties were thus reminiscent of known β-chloroketones of the aliphatic series [2]. On repeated distillation nearly the whole came over at 115-120° (1 mm); d_4^{20} 1.1130; n_D^{20} 1.5326. Yield 23.1% of theory, calculated on the total ketone used, and about 47% calculated on the reacted ketone.

0.1814 g substance: 0.1300 g AgCl. 0.1608 g substance: 0.1155 g AgCl. 0.1620 g substance: 18.41 g C_6H_6: Δt 0.262°. 0.1473 g substance: 14.75 g C_6H_6: Δt 0.290°. Found %: Cl 17.69, 17.72; M 176, 181. $C_{10}H_{11}OCl$. Calculated %: Cl 19.45; M 182.5.

The low halogen content found may be due to partial hydrolysis of the chloromethylated product during washing (as well as to partial cleavage of HCl during the distillation).

Oxidation: The position of the CH_2Cl group in the molecule of the prepared product was determined by oxidation. 2.4 g product was emulsified with 22 ml 17% sodium hydroxide solution and addition was made at room temperature in small portions of 262 ml 5% $KMnO_4$. The mixture was then heated on the water bath (60-70°) for 4 hours. The excess of permanganate was deoxidized by careful addition of formaldehyde solution. The filtered precipitate was twice digested with water (50 ml each time). The aqueous extracts were combined with the filtrate, and the solution, after concentration on the water bath to a volume of 50 ml, was filtered through a small filter; the residue on the filter was washed 3 times with water (about 2-2.5 ml portions). Acidification of the filtrate with 10% H_2SO_4 caused a fine crystalline precipitate to separate. The precipitate dissolved when heated, and on slow cooling well-formed colorless platelets crystallized out. Yield of air-dry crystals 1.25 g or 78.1% of the theoretical; m.p. 118-122° and, after sublimation, 119-121.5°. A sample did not depress the melting point of benzoic acid. Titration with alkali confirmed that benzoic acid had been prepared. This also served as evidence that the CH_2Cl group is not introduced into the ring but into the side-chain, so that the obtained compound must have the structure: $C_6H_5COCH(CH_3)CH_2Cl$.

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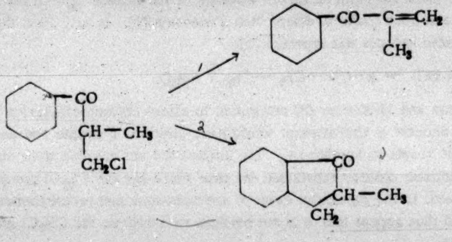
* BF_3 has not previously been applied as a catalyst in the chloromethylation reaction.

** The reaction failed when using purer monochlorodimethyl ether (b.p. 54-60°) as the chloromethylating agent. The reason for this remains unexplained.

Cleavage of HCl. Two reactions are possible in the cleavage of HCl:

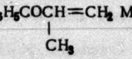


The possibility of the second direction is confirmed to some extent by the analogy with Fuson's experiment [5] when cleavage of water from methylolpropiophenone $C_6H_5COCH(CH_3)CH_2OH$ gave α-methylhydrindone instead of the expected phenylisopropenyl ketone.

5.45 g chloromethylated ketone and 5 g quinoline (m.p. 234-238°) were heated in a flask under a reflux condenser, protected with a $CaCl_2$ tube, at 70-80° (water bath) for 4 hours. The mixture was then distilled in vacuum when 6.32 g came over at 90-92° (1 mm), leaving a residue of 3.29 g (loss 0.46 g).

The distillate was washed with 5% HCl (to remove any quinoline which distilled over) and then with water until the reaction for halogen was negative. The washed distillate was dissolved in ether and dried with freshly calcined sodium sulfate. Removal of the ether left a colorless, transparent liquid with a negative reaction for halogen (Beilstein test). Yield 3.33 g or 76.2% of theory. Its pungent odor and irritant action on the eyes were strongly reminiscent of the commonest, simplest vinyl ketones (methyleneacetone, etc.).

d_4^{20} 1.0103; n_D^{20} 1.5342; MR_D 44.93.



$$\underset{\displaystyle CH_3}{C_6H_5COCH{=}CH_2}$$

MR_D 44.32; α-methylhydrindone MR_D 42.59.

Oxidation (by the above-described method) gave benzoic acid in a yield of 52% of the theoretical. Phthalic acid would have been formed in the case of α-methylhydrindone, but was not found here. There was consequently no further doubt that, at any rate for the most part, the cleavage of HCl took place in direction 1 (see scheme above) and that the product was isopropenylphenyl ketone.

2. Chloromethylation of acetophenone. Following the experiment with propiophenone the chloromethylation of acetophenone (51.28 g, b.p. 201-204°) was performed by the same procedure except that the heating on the water bath at 60-65° lasted only 11 hours (due to the marked darkening of the mixture) instead of 31 hours (and 1 hour at 80°).

The washed and dried product (53.72 g) was vacuum-fractionated and gave: Fraction 1, 88-96° (12mm), 36.77 g; fraction 2, 96-107° (12 mm), 7.28 g; residue (viscous amber-colored resin), 8.94 g; loss 0.73 g.

A fresh distillation of the first fraction brought it over at 83-86° (11 mm); this was unreacted acetophenone. The second fraction was strongly reminiscent of the second fraction [b.p. 124-134° (6.5 mm)] of the preceding experiment: a colorless liquid with a pungent odor, fuming in the air, and darkening on standing. It gave a positive reaction in the Beilstein halogen test.

When redistilled it almost completely polymerized* (unexpectedly) to an undistillable, transparent, viscous mass with an amber color; only about 1 g distillate was obtained, while a small quantity of halogen-containing

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[*] This fact alone is clear evidence that chloromethylation had taken place not at the ring but at the side-chain, since it is impossible to expect that compounds of the type of $ClCH_2C_6H_4COCH_3$ would polymerize so easily, or, indeed, that they would show any tendency at all to polymerize.

material crystallized at the end of the side tube of the distillation flask. After pressing on porous tile, the crystals melted at 46-49°. According to the literature [6] β-chloropropiophenone $C_6H_5COCH_2CH_2Cl$ melts at 57° and when distilled it partially changes into vinylphenyl ketone $C_6H_5COCH = CH_2$. It was clear in the light of all these facts that the product in the second fraction was mainly β-chloropropiophenone, i.e., in the case also of acetophenone the chloromethylation reaction took place and the CH_2Cl group entered the side chain.

Oxidation of the polymerized product gave benzoic acid in a yield of about 40% of the theoretical. Therefore these data likewise confirm out conclusion, for if chloromethylation had taken place at the ring, the structural unit of the polymer would have been a benzene ring with two side chains, and oxidation of such a polymer would have yielded phthalic acids.

SUMMARY

1. Side-chain chloromethylation was effected of acetophenone and propiophenone, although these compounds are reported in the literature to be not at all amenable to chloromethylation.

2. Cleavage of HCl from β-chloroisopropylphenyl ketone gave phenylisopropenyl ketone in 76% of the theoretical yield. The latter compound has not been described in the literature.

3. Boron fluoride etherate was used, for the first time, as catalyst in the chloromethylation.

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NEW OXIDATION REDUCTION INDICATORS

III. p- AND m-N-PHENYLAMINOBENZOIC ACIDS

V. M. Cherkasov

In one of the preceding publications [1] phenylanthranilic acid was proposed, for the first time, as an oxidation-reduction indicator. Within a short period phenylanthranilic acid found wide application in analytical chemical practice as an indicator with a high potential, and is now in general use. It was therefore natural that the possibility of using the isomers of phenylanthranilic acid, i.e., m- and p-phenylaminobenzoic acids, as oxidation-reduction indicators should be investigated. A comparative study of the three isomeric phenylaminobenzoic acids as oxidation-reduction indicators is also of theoretical interest, for such a study is bound to give some information on the dependence of the oxidation-reduction potential on the relative positions of the phenylamino and carboxyl groups in the benzene ring. Strange as it may seem, m- and p-N-phenylaminobenzoic acids have not hitherto been investigated, although attempts to prepare them have been reported in the literature [2].

The purpose of the present research was the preparation of m- and p-phenylaminobenzoic acids and of some of their derivatives and an exploratory study of these new compounds as oxidation-reduction indicators.

Goldberg [2] unsuccessfully attempted to prepare m- and p-phenylaminobenzoic acids by the action of m- and p-chlorobenzoic acids on aniline, or by the action of m- and p-aminobenzoic acids on bromobenzene in presence of copper powder. We, too, failed to obtain m- and p-phenylaminobenzoic acids when we repeated Goldberg's experiments.

It is known that the phenylation of aromatic amines proceeds most readily of all with aryl iodides [3,4], and least readily with aryl chlorides; we therefore decided to attempt the preparation of m- and p-phenylaminobenzoic acids by using the corresponding iodo compounds. By reacting iodobenzene with m- and p-aminobenzoic acids in presence of Cu powder, we prepared m- and p-phenylaminobenzoic acids, but only in low yields (~4%). Somewhat better yields 15, 17%) are obtained by the action of aniline on m- and p-iodobenzoic acids in presence of Cu powder.

p-Phenylaminobenzoic acid is a colorless crystalline compound with m.p. 158-159°; m-phenylaminobenzoic acid melts at 141-142°. Both acids are good oxidation-reduction indicators with a potential of about 1.12 V, i.e., very close to the oxidation-reduction potential of phenylanthranilic acid*. Consequently the position of the carboxyl in relation to the phenylamino group has no great influence on the magnitude of the oxidation-reduction potential. m- and p-Phenylaminobenzoic acids have no advantages over phenylanthranilic acid as oxidation-reduction indicators.

p-Phenylaminobenzoic acid was characterized by the preparation of its methyl ester and its hydrazide. Both of these substances gave a coloration with oxidizing agents in acid solutions, but they are unsuitable as indicators because the coloration is irreversible.

In conclusion we thank Professor A. V. Kirsanov sincerely for his advice during this investigation.

EXPERIMENTAL

p-N-Phenylaminobenzoic acid. A mixture of 9 g p-iodobenzoic acid, 9 g anhydrous potassium carbonate, 40 ml freshly distilled aniline and 0.2 g copper powder was refluxed under an air condenser for 15 hours. The aniline was distilled off in steam and the solution was filtered and acidified with hydrochloric acid. The precipitate was drained, washed with water and dried. p-Iodobenzoic acid was removed by treating the dry precipitate several times with hydrochloric acid sp. gr. 1.19.

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*Oxidation-reduction potentials were determined by V.S. Syrokomsky and V.V. Stepin in the laboratory of the Ural Institute of Heavy Metals.

The drained acidic filtrate was diluted with water, the precipitate was drained and washed with water. The dry substance was dissolved in cold benzene, the solution was treated with active carbon, the benzene was distilled off, and the crystalline residue, light yellow in color, was twice recrystallized from aqueous alcohol. Yield of pure product about 15% of the theoretical. p-N-Phenylaminobenzoic acid forms colorless needles, soluble in ether and benzene, less easily soluble in alcohol, and soluble with difficulty in water. M.p. 158-159° (uncorr.).

9.482 mg substance: 0.550 ml N_2 (11°, 746 mm). Found%: N 6.69. $C_{13}H_{11}O_2N$. Calculated %: N 6.56.

Methyl ester of p-N-phenylaminobenzoic acid. Methylation with dimethyl sulfate. 0.01 mole (2.13 g) p-N-phenylaminobenzoic acid was shaken for 15 minutes with 5.5 ml of 2 N sodium hydroxide and 1.40 g dimethyl sulfate, after which the mixture was heated on the water bath for 30 minutes. On cooling, 1.27 g crystalline product came down. Crystallization from ethyl alcohol gave the methyl ester of p-N-phenylaminobenzoic acid in the form of colorless needles with m.p. 115-116°; sparingly soluble in water, soluble in ether and benzene.

Methylation with diazomethane. To 1 g p-N-phenylaminobenzoic acid was added 60 ml of a solution of diazomethane in ether (from 5 ml nitrosomethylurethane). After the acid has dissolved, another 30 ml of solution of diazomethane in ether (from 2.5 ml nitrosomethylurethane was added. The ether was distilled off and the methyl ester of p-N-phenylaminobenzoic acid was recrystallized from alcohol to form colorless needles with m.p. 115-116°. It did not depress the melting point of the methyl ester prepared by reacting methyl sulfate with p-N-phenylaminobenzoic acid.

10.121 mg substance: 0.57 ml N_2 (12°, 747 mm). Found %: N 6.49. $C_{14}H_{13}O_2N$. Calculated %: N 6.26.

Hydrazide of p-N-phenylaminobenzoic acid. 0.45 g methyl ester of p-N-phenylaminobenzoic acid was heated on the water bath with excess of hydrazine hydrate for 5 hours. The cooled reaction mixture was diluted with water and acidified with dilute hydrochloric acid. The hydrazide of p-N-phenylaminobenzoic acid was precipitated from the solution with potassium hydroxide and after recrystallization from alcohol had m.p. 193-194°.

5.254 mg substance: 0.87 ml N_2 (13°, 740 mm). Found %: N 18.81. $C_{13}H_{13}ON_3$. Calculated %: N 18.50.

m-N-Phenylaminobenzoic acid. A mixture of 0.06 mole (14.7 g) m-iodobenzoic acid, 10 g potassium carbonate, 50 ml aniline and 0.2 g copper powder was refluxed under an air condenser for 15 hours. The aniline was distilled off in steam and the solution filtered and acidified with hydrochloric acid. The dry precipitate was extracted several times in the cold with benzene until the benzene-insoluble product failed to give a blue-violet color with bichromate in sulfuric acid. Distillation of the benzene left a yellow oil which crystallized after two days. The product was treated with sodium carbonate solution. The insoluble portion (the main mass) after washing with water did not give a coloration with bichromate. The product was precipitated from the sodium carbonate solution with hydrochloric acid; a brown oil separated out which was dissolved in acetone. After filtration, the acetone was distilled off and the oily residue was treated with several lots of boiling water. The combined aqueous extracts were treated with active carbon and filtered; crystals came out which were recrystallized until the m.p. was constant at 140-141°. m-N-Phenylaminobenzoic acid forms colorless prisms, readily soluble in ether and acetone, less readily soluble in benzene and alcohol. 0.9 g pure product was obtained, or 7% of the theoretical yield.

6.984 mg substance: 0.41 ml N_2 (15°, 742). 11.310 mg substance. 0.67 ml N_2 (15°, 742 mg). Found %: N 6.66, 6.71. $C_{13}H_{11}O_2N$. Calculated %: N 6.56.

Test of indicators. Indicator tests were performed with 0.001 N potassium bichromate, 0.001 M solutions of indicators prepared by dissolving 0.213 g p- and m-N-phenylaminobenzoic acids and 0.1 g sodium carbonate in 1 liter water. The total volume of the test solution was 100 ml. Following the earlier procedure [2] the following characteristics were determined: 1) limit of acidity (normality of sulfuric acid) at which the color of the indicator is sufficiently intense for titration; 2) minimum amount of indicator; 3) minimum amount of oxidizing agent; 4) stability and reversibility of the indicator. During the oxidation of p-N-phenylaminobenzoic acid the color changes from colorless through green to blue-violet. With m-N-phenylaminobenzoic acid the color changes from green to blue-violet through pink and the final color is weaker than that of the p-isomer. The results are given in the table.

When oxidation was performed with cerium sulfate a sufficiently intense color of the indicators is developed at a much lower acidity (in 2 N sulfuric acid). If excess of oxidizing agent is added to a solution containing ions of divalent iron, then the color of the indicators is developed at lower acidity. Consequently titration of Mohr's salt with both indicators is possible in 5-6 N sulfuric acid. The indicator error was determined by titrating solutions of Mohr's salt with bichromate in presence of the new indicators side by side with titrations with diphenylaminesulfonic acid and phenylanthranilic acid. Identical results were obtained.

TABLE

Acid	p-Phenylaminobenzoic acid	m-Phenylaminobenzoic acid
oxidation-reduction potential	1.12 V	about 1.12V
acidity at which color is developed	3 N	2 N pale green
change of color with increased acidity	6.5 N pale violet	5.0 N develops pink color 6.5 N intense pink color 7.5 N pale violet color, rapidly changing to pink
limit of acidity	7.5 N optimum 9 N	9 N blue-violet color optimum 10 N
minimum of oxidizing agent in optimum conditions	1 ml optimum 2 ml	1 ml optimum 2 ml
minimum amount of indicator	1 ml	1.5 ml
color stability in optimum conditions	12 hours	1 hour

SUMMARY

1. p- and m-N-phenylaminobenzoic acids have been synthesized.

2. It is shown that the introduction of the carboxyl group into the diphenylamine molecule considerably increases the oxidation-reduction potential of the indicator, and the position of the carboxyl group hardly influences the oxidation-reduction potential.

3. m- and p-N-phenylaminobenzoic acids can be applied in titration with strong oxidizing agents such as bichromate and salts of tetravalent cerium.

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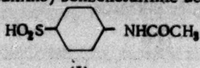
STUDIES ON QUINONES

I. REACTION OF p-BENZOQUINONE WITH ACYLAMINOSULFINIC ACIDS

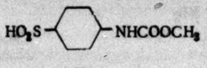
I. S. Ioffe

It is over 100 years since the discovery of p-benzoquinone by the "father of Russian chemistry", A. A. Voskresensky. This compound was the forerunner of a large group of quinones of great theoretical and practical importance. Among quinone derivatives we may include dyes, both natural and synthetic. Many natural organic compounds possessing physiological activity are also quinone derivatives. Quinones have therefore attracted considerable attention and have been the object of numerous investigations. Nevertheless the reactions of these chemically very active compounds have not been exhausted. Descriptions of new quinone reactions are frequently appearing in the literature and many of these reactions have not been sufficiently developed. This is true of the reaction of quinone with sulfinic acids, described for the first time in 1894 by Ginsberg [1].

We have made a study of the products of reaction of p-benzoquinone with acylaminobenzenesulfinic acids, which are genetically related to sulfanilamide, in particular with p-acetylaminobenzenesulfinic acid (I) and p-(methoxycarbamino)-benzenesulfinic acid (II).



(I)

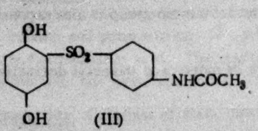


(II)

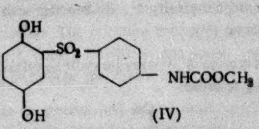
p-Acetylaminobenzene sulfinic acid [2] is prepared by reduction of p-acetylaminobenzene sulfochloride with sodium sulfite. In similar conditions, starting from the p-sulfochloride of methoxycarbaminobenzene (phenylurethylane), we prepared the previously undescribed sulfinic acid (II).

These sulfinic acids enter very quickly into reaction with p-benzoquinone. The resultant products are almost completely insoluble in hot water. We exploited this property in developing a very simple method for the nearly quantitative preparation of products of reaction of p-benzoquinone with the aforementioned sulfinic acids. To a boiling aqueous solution of the latter is added the finely pulverized quinone in small portions and with energetic stirring. Addition of each portion of quinone is marked by the appearance of a yellow color in the solution, but this disappears almost instantaneously and a colorless condensation product is precipitated.

Analyses and an examination of the properties of the products showed that they were formed by the addition to one molecule of quinone of one molecule of sulfinic acid (I) or (II). Such addition products contain an unchanged acylamino group and, as shown by quantitative acetylation, two hydroxyl groups. This proves that addition of sulfinic acids to the quinone takes place through the sulfinic groups with formation of 4-acylamino-2', 5'-dihydroxydiphenylsulfones with the structures (III) and (IV) respectively.

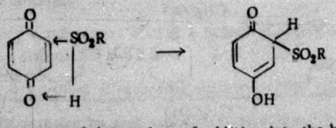


(III)



(IV)

These compounds are probably formed by the scheme common to quinones:

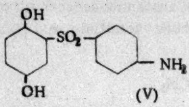


with rearrangement of the product of addition into the hydroxy derivative (III) or (IV).

Quinones react according to this scheme with other compounds, for example, amines. In the majority of cases, however, the reaction does not stop at formation of the hydroquinone derivative, since the latter is oxidized by the original quinone with formation of still another new quinone derivative which is either precipitated or enters into reaction with a fresh molecule of the reaction component. The consequence is that the yield of condensation product does not exceed 50 or 33% (depending on the number of combining residues) of the amount of initial quinone.

In the condensation of quinone with sulfinic acids, however, the reaction stops at the stage of formation of the hydroquinone derivative and the yield of this product approaches 100%. This difference in the course of reaction of quinone with sulfinic acids is explained, on the one hand, by the fact that the formed hydroquinone derivative is substantially insoluble in hot water and is precipitated, and, on the other hand, by the fact that quinone derivatives containing sulfone residues possess higher oxidation potentials than unsubstituted quinones. Thus, according to Fieser's data [3], in the α-naphthoquinone series the introduction of the tolylsulfonic residue raises the oxidation potential by 121 mV. Hence quinone derivatives containing sulfonic residues must possess stronger oxidizing properties than unsubstituted quinones. In the case under discussion, therefore, the quinone no longer oxidizes the hydroquinone derivatives (III) or (IV).

These two compounds differ in the character of the radical which acetylates the amino group. Their saponification yields one and the same amino compound, 4-amino-2', 5'-dihydroxydiphenylsulfone (V). The acetyl derivative (III) is readily saponified by both hydrochloric acid and caustic alkali. But the acyl derivative (IV) is not saponified by acid and remains unchanged even after prolonged boiling with hydrochloric acid; it is only saponified by alkali.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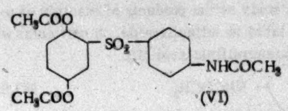
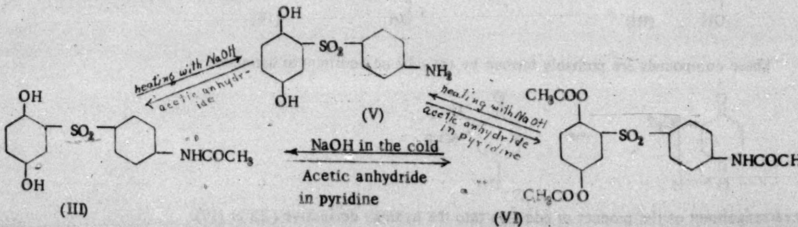

(VI)

The amino compound (V) is soluble in hot water. The best medium for crystallization of the compound is dilute alcohol. Colorless crystals are thus obtained with m.p. 175-176° which are soluble both in dilute caustic alkali and in dilute hydrochloric acid. The hydrochloride of 4-amino-2', 5'-dihydroxydiphenylsulfone is prepared by dissolving the amine in hot 10% hydrochloric acid and then cooling the solution. It comes down in the form of colorless crystals with m.p. 208-210°. The hydrochloride hydrolyzes in water with separation of the free amine.

Gentle heating of the amino compound with acetic anhydride leads to acetylation of only the amino group with formation of 4-acetylamino-2', 5'-dihydroxydiphenylsulfone (III), which forms colorless crystals, m.p. 282-285°, identical with the product of condensation of quinone with acetylaminobenzene sulfinic acid. Acetylation with a mixture of acetic anhydride and pyridine leads to acetylation not only of the amino group but also of the hydroxy groups with formation of a triacetyl derivative (VI). In contrast to the monoacetyl derivative (III), the triacetyl derivative (VI) is soluble in hot alcohol; it crystallizes in the form of colorless crystals which melt at 180-182°. The same triacetyl derivative is obtained by acetylation with acetic anhydride in pyridine of the monoacetyl derivative (III).

The triacetyl derivative (VI) slowly goes into solution when treated with cold caustic alkali solution. During this operation only the acetoxy groups are saponified and acidification of the solution leads to precipitation of 4-acetamino-2',5'-dihydroxydiphenylsulfone. By heating with alkali the acetamino group is also saponified with formation of the amino compound (V).

The interrelations of 4-amino-2',5'-dihydroxydiphenylsulfone with its mono- and triacetyl derivatives may be represented by the following scheme:



EXPERIMENTAL

I. 4-Acetylamino-2',5'-dihydroxydiphenylsulfone (III).

a) Preparation. 20 g p-acetaminobenzenesulfinic acid is dissolved in 500 ml boiling water. The solution is filtered, again brought to the boil and addition is made, in small portions, of 11 g p-benzoquinone with good stirring. During the introduction of each portion of the quinone the solution turns orange-yellow, but this color vanishes almost at once. The solution rapidly begins to deposit the colorless condensation product, the quantity of which steadily increases. Toward the end of the experiment the quinone is added in extremely small portions. When at a certain moment the color does not disappear, addition is made to the suspension of a few milliliters of a solution of acetaminobenzenesulfinic acid until decolorization is complete. The suspension is then boiled for a further 15 minutes, after which the precipitate is filtered, washed on the filter with hot water, and dried. Yield 30 g, which is very close to the theoretical.

b) Properties. The compound is very poorly soluble in organic solvents, almost completely insoluble in water. It dissolves readily in dilute caustic alkali solutions with formation of a pale yellow solution which when acidified deposits the original compound in the form of slender, colorless needles (as viewed under the microscope). Heating of the alkaline solution causes saponification with formation of the amino compound. It also saponifies when heated with inorganic acids. It crystallizes from large volumes of acetic acid or alcohol in the form of colorless needles melting at 282-285° after darkening.

0.1322 g substance: 0.0978 g $BaSO_4$. 0.1622 g substance: 0.1214 g $BaSO_4$. Found %: S 10.20, 10.29. $C_{14}H_{13}O_5NS$. Calculated %: S 10.40.

Determination of hydroxyl groups by quantitative acetylation.

0.0030 g substance: 6.9 ml 0.1 N NaOH. 0.1246 g substance: 3.3 ml 0.1 N NaOH. Found %: OH 11.28, 11.32. $C_{14}H_{11}O_3NS(OH)_2$. Calculated %: OH 11.08.

II. 4-Acetylamino-2',5'-diacetoxydiphenylsulfone (VI).

a) Preparation. 3.1 g 4-acetoxy-2',5'-dihydroxydiphenylsulfone is introduced into a mixture of 40 g pyridine and 10 g acetic anhydride. The precipitate goes into solution when heated on the water bath. Heating on the water bath is continued for a further hour, after which the nearly colorless solution is poured into 300 ml hot water. On cooling, the acetylation product separates in the form of needles. These are filtered, washed with water and then crystallized from aqueous alcohol. Yield of crystalline substance 2.5 g or 64% of the theoretical.

b) Properties. The compound is highly soluble in hot water, alcohol and acetic acid. It crystallizes from slightly aqueous alcohol or from pure alcohol in the form of colorless, beautifully formed, slender needles. It melts sharply at 182-184°. It dissolves slowly in cold caustic alkali solution with saponification of the acetoxy groups. Acidification of this alkaline solution brings down 4-acetylamino-2',5'-dihydroxydiphenylsulfone with m.p. 282-285°. Heating with alkali causes saponification also of the acetamino group with formation of the amino compound.

0.1560 g substance: 0.0924 g $BaSO_4$. 0.1542 g substance: 0.0934 g $BaSO_4$. Found %: S 8.13, 8.3
$C_{18}H_{17}O_7NS$. Calculated %: S 8.18.

III. 4-Methoxycarbamino-2',5'-dihydroxydiphenylsulfone (IV).

a) Preparation. 22 g p-methoxycarbaminobenzenesulfinic acid, prepared by reaction of p-methoxycarbaminobenzenesulfochloride with sodium sulfite, is dissolved in 500 ml boiling water, and to the filtered solution is added, with boiling and good stirring, 11 g p-benzoquinone. The reaction proceeds as in that of quinone with p-acetylaminobenzenesulfinic acid. The reaction product, poorly soluble in hot water, comes out of solution; it is filtered, washed with hot water and dried. Yield 32 g or 97% of the theoretical.

b) Properties. Colorless crystals, poorly soluble in alcohol and acetic acid, sparingly soluble in hot water from which it crystallizes on cooling; m.p. 210-211°. Very stable when heated with inorganic acids and, unlike 4-acetylamino-2',5'-dihydroxydiphenylsulfone, is not saponified in these conditions. It only saponifies when heated with caustic alkalies.

0.1566 g substance: 0.1118 g $BaSO_4$. 0.1536 g substance: 0.1114 g $BaSO_4$. Found %: S 9.81, 9.96. $C_{14}H_{13}O_6NS$. Calculated %: S 9.91.

IV. 4-Amino-2',5'-dihydroxydiphenylsulfone (V).

a) Preparation by acid saponification of 4-acetamino-2',5'-dihydroxydiphenylsulfone. 30 g 4-acetamino-2',5'-dihydroxydiphenylsulfone is introduced into 150 ml 10% hydrochloric acid and the suspension is heated at the boil in a flask under a reflux condenser until the precipitate dissolves completely. The solution is evaporated to dryness on the water bath. The dry precipitate is dissolved in 200 ml hot water to which is added a small quantity of hydrochloric acid, and the obtained solution is filtered after treatment with animal charcoal. The filtrate is stirred into a hot solution of 30 g sodium acetate in 200 ml water. The amino compound separates as colorless flocs which are stood for 12 hours and then filtered, washed with water and dried. Yield 22 g or 83% of the theoretical.

b) Preparation by alkaline saponification of 4-acetamino-2',5'-dihydroxydiphenylsulfone. 30 g 4-acetamino-2',5'-dihydroxydiphenylsulfone is dissolved in 150 ml 10% sodium hydroxide and the solution is brought to the boil. The completion of the reaction is recognized by the formation of a transparent solution when hydrochloric acid is added to a sample. Addition is then made to the reaction mass of 50 ml 20% acetic acid; after standing for 12 hours the amino compound comes down and is filtered, washed with water and dried. Yield 23 g or 85% of the theoretical.

c) Preparation by alkaline saponification of 4-methoxycarbamino-2'-5'-dihydroxydiphenylsulfone. 32 g of the methoxycarbamino compound is dissolved in 150 ml 10% sodium hydroxide and the saponification is conducted as in the preceding experiment. Yield of product the same.

d) Properties. Colorless crystalline substance. Readily soluble in alcohol and acetic acid; slightly soluble in hot water. Crystallizes nicely from aqueous alcohol on addition of traces of bisulfite. Melts with darkening at 175-176°. Forms a hydrochloride which crystallizes from 10% hydrochloric acid in the form of colorless crystals. Gentle heating with acetic anhydride converts it into 4-acetamino-2',5'-dihydroxydiphenylsulfone, separating as crystals with m.p. 282-285°. Heating with acetic anhydride in presence of pyridine converts it into 4-acetamino-2',5'-diacetoxydiphenylsulfone which melts at 180-182° after crystallization from aqueous alcohol. The compound is soluble in caustic alkalies, but the alkaline solutions gradually darken on standing. The aqueous solutions turn brown when treated with oxidizing agents and a brown precipitate is formed.

0.1344 g substance: 0.1188 g $BaSO_4$. 0.1120 g substance: 0.0980 g $BaSO_4$. Found %: S 12.14, 11.82. $C_{12}H_{11}O_4NS$. Calculated %: S 12.8.

e) Hydrochloride. Formed by dissolving the amino compound in hydrochloric acid. Crystallizes from 10% hydrochloric acid solution as colorless crystals, m.p. 208-210°. It is easily hydrolyzed in water from which the amino compound, m.p. 175-176°, comes down. The salt is stable when kept in a desiccator in the dry state.

SUMMARY

Reaction of p-benzoquinone with acylaminobenzenesulfinic acids yields colorless products of condensation of equimolar amounts of the starting components, possessing the structure of 4-acylamino-2',5'-dihydroxydiphenylsulfone. Saponification gives 4-amino-2',5'-dihydroxydiphenylsulfone. Mild acetylation of the latter leads to acetylation of only the amino group, but acetylation with acetic anhydride in pyridine leads to acetylation also of the hydroxy groups with formation of the triacetyl derivative – 4-acetylamino-2',5'-diacetoxydiphenylsulfone. Only the acetoxy groups are saponified by treatment with cold alkali solution. Full saponification occurs on heating with alkali and 4-amino-2',5'-dihydroxydiphenylsulfone is formed.

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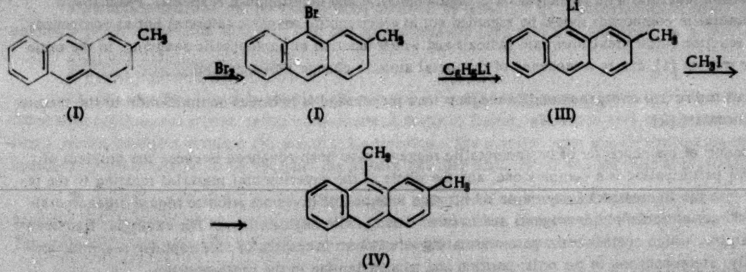
ORIENTATION PHENOMENA IN SUBSTITUTION REACTIONS WITH PARTICIPATION OF ORGANIC COMPOUNDS OF ALKALI METALS

B. M. Mikhailov and V.P. Bronovitskaya

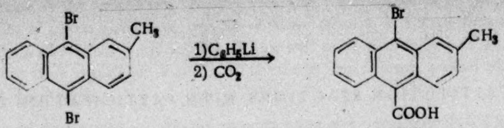
With the aim of throwing light on the controversial question as to whether organic compounds of the alkali metals are to be regarded as electrophilic or nucleophilic reagents, we undertook a study of orientation phenomena in reactions with participation of bromine and phenyllithium in the anthracene series. Anthracene derivatives are convenient materials from the systematic standpoint.

Starting materials were 2-methylanthracene and 2-methyl-9,10-dibromoanthracene. When one equivalent of bromine was reacted with a carbon bisulfide solution of 2-methylanthracene (I), one of two possible mesoisomers, 2-methyl-9-bromoanthracene (II), was separated in 63% yield, which fact permits the conclusion that substitution takes place mainly in the 9-position. The structure of the bromo compound (II) was established by its transformation into the dimethyl compound by replacing the bromine atom by lithium followed by reaction of the organolithium compound (III) with methyl iodide. The resultant hydrocarbon was 2,9-dimethylanthracene (IV), identical with the hydrocarbon formed by the Grignard reaction between methyl magnesium iodide and 2-methylanthrone-9:



Having established the orientating effect of a substituent of the first order in relation to the electrophilic reagent (bromine), we turned our attention to the second half of the problem – the elucidation of the direction of reaction with participation of an organometallic compound (phenyllithium). In this connection we did not study the hydrogen-lithium exchange reaction (metalation) – the usual procedure up to now – but the halogen-metal exchange reaction, and more precisely the action of phenyllithium on 2-methyl-9,10-dibromoanthracene. Our selection of this type of reaction was influenced by the consideration that replacement of hydrogen atoms by bromine in the 2-methylanthracene molecule does not change the relative electro-negativity of the meso-carbon atoms and consequently does not reflect the direction of reaction with the organometallic reagent, whereas replacement of halogen by metal proceeds more quickly and completely and is not complicated by intermediate reactions as is the case with metalation when, for example, toluene is first metalated at the methyl group and subsequent metalation in the ring is governed not by the methyl group but by the methyl-metal group.

Reaction of one equivalent of phenyllithium with 2-methyl-9,10-dibromoanthracene (V) followed by hydrolysis of the formed isomeric organolithium compounds gave one of the two possible isomers, 2-methyl-9-bromoanthracene (II), but the low yield (24%) did not permit a decision as to whether the preferred course of the halogen-metal exchange reaction was at the 9- or the 10- position. The products of reaction of phenyllithium with 2-methyl-9,10-dibromoanthracene were then subjected to carboxylation, and from the obtained carboxylic acids we were able to isolate an acid (m.p. 238°) in the pure form in a yield of 59% of the theoretical. This acid proved to have the structure of 2-methyl-9-bromoanthracene-10-carboxylic acid (VI). This structure was established by comparison with a specimen of the isomeric acid, 2-methyl-10-bromoanthracene-10-carboxylic acid (VIII).

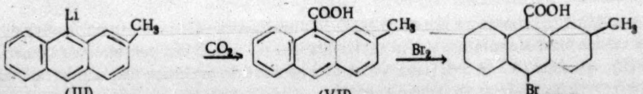


(V) (VI)

The latter was prepared by the following series of transformations which left no doubt about its structure.

Treatment of 2-methyl-9-bromoanthracene (II) with n-butyllithium gave the organolithium compound (III); carboxylation of the latter gave 2-methylanthracene-9-carboxylic acid (VII), which was converted by bromination into acid (VIII) with m.p. 230.5° The position of the bromine in the acid was confirmed by oxidation to 2-methylanthraquinone.

A mixed sample of acids (VI) and (VIII), whose melting points are fairly close, had a lower melting point.



(III) (VII) (VIII)

Hence the action of phenyllithium on 2-methyl-9, 10-dibromoanthracene is marked by preferential substitution by lithium of the bromine atom in the 10-position, i.e., the methyl group manifests an opposite orientating influence in substitution reactions with participation of organometallic and electrophilic reagents. From this it follows that organometallic compounds should be regarded not as electrophilic reagents (Morton) but as compounds which in course of reaction suffer breakdown into radicals and which function as nucleophilic reagents, in the same manner as metallic sodium [1], due to a tendency of the metal atom to change into a cation.

The theory of the nature of organometallic reagents here propounded is in direct contradiction to the theories enunciated in the literature [2].

Various concepts of the character of organometallic reagents have been advanced because the problem of orientation with their participation is a complex one, and the whole of the experimental material relating to the reactions does not fit into the framework of any single substitution scheme, and gives occasion to regard organometallic compounds sometimes as nucleophilic reagents and in other cases as electrophilic ones. For example, fluorobenzene and triphenylamine, which contain ortho-para-orientating substituents in respect of electrophilic reagents, are metalated differently: fluorobenzene in the ortho-position and triphenylamine in the meta-position.

The totality of conflicting phenomena of substitution in metalation processes can be reconciled and systematized if we assume that in the final organometallic compounds containing alkali metal in the ortho-position to an electronegative substituent, as for example in o-lithium-fluorobenzene, there is effected a bond between metal and heteroatom similar in character to the hydrogen bond. Formation of a hydrogen-like bond between metal and heteroatom energetically stabilizes the system and is therefore a thermodynamic factor promoting the substitution reaction in the ortho position.

The theory propounded above appears entirely plausible if we consider that, first, the distance between the alkali metal and the heteroatom when in the ortho-position to each other, for example in o-lithium-fluorobenzene or o-lithium-anisole, is of the same order (2.75 A) as in compounds containing a typical hydrogen bond (2.25-3 A), and, second organic compounds of alkali metals tend to form complexes [3]. The justification for postulating the occurrence of a hydrogen-like interaction between the alkali metal and the atom of the electronegative element is founded on the totality of metalation reactions of variously constituted aromatic and heterogeneous compounds. A comparison of the factual material relating to this field of transformations leaves no doubt also that in cases when the reaction course is not complicated by the supplementary effects of hydrogen-like interactions of the substituents, the organometallic compounds behave unmistakably like nucleophilic reagents.

Indeed in compounds with ortho- and para-orientations which are electropositive (in phenyllithium and benzylsodium) or weakly electronegative (in triphenylamine, triphenylarsine and triphenylphosphine) metalation takes place in the meta-position. In all compounds, however, with strongly electronegative substituents capable of entering into reaction with alkali metals, substitution takes place in the ortho-position.

Compounds of the latter type fall into two groups. First, we have compounds containing ortho- and para-directive substituents and undergoing substitution under the action of both electrophilic and organometallic reagents in the ortho-position, and therefore justifying the classification of organic compounds of the alkali metals as electrophilic reagents. Examples are fluorobenzene, aniline, sodium phenolate, anisole, furane, thiophene and a series of other compounds.

The second group will include representatives of the benzene, diphenyl and heterocyclic series. In these no consistency of orientation is observed when using electrophilic and metalating reagents. In this group of compounds substitution under the action of the latter reagents likewise takes place in the ortho-position to the heteroatom.

As examples we may cite the transformations of diphenyl ether (metalation in the 2-position [4], halogenation in the 4-position [5]) dibenzofuran (metalation in the 1-position [6,4], halogenation in the 3-position [7,8]) and many other compounds.

EXPERIMENTAL

2-Methylanthracene. 5 g 2-methylanthraquinone, 4.5 g granulated tin and 34 ml glacial acetic acid are heated to boiling in a flask under a reflux condenser. Addition is made to the boiling solution over a period of two hours of 11.5 ml concentrated hydrochloric acid (sp.gr.1.19) in 1 ml portions. The reaction mass is then diluted with 50 ml water and the yellow precipitate is filtered off.

A mixture of the prepared methylanthrone, 6 g zinc dust and 100 ml 2 N NaOH was boiled for 3 hours. The precipitate was filtered and treated with 10% hydrochloric acid for removal of unreacted zinc dust. The obtained hydrocarbon was crystallized from benzene-alcohol. M.p. 208-209°. Yield 72.7%.

2-Methylanthracene has previously been prepared by reduction of 2-methylanthraquinone with zinc dust and ammonia [9] or by heating with zinc dust at high temperature [10]; yields not specified, m.p. 207°.

2-Methyl-9-bromoanthracene:

a) To a carbon bisulfide solution (75 ml) of 3 g 2-methylanthracene (cooled to 0°) in a three-necked flask fitted with mechanical stirrer, reflux condenser and dropping funnel, was added very slowly and with energetic stirring a carbon bisulfide solution (15 ml) of 2.5 g bromine. The reaction mass was then stirred on the water bath until hydrogen bromide ceased to be evolved; the solvent was then distilled off and the residue crystallized from alcohol.

There was obtained 2.8 g of a substance with m.p. 84-91°; a less pure fraction was recovered from the partially concentrated mother liquor, and after crystallization from dioxane-alcohol it melted at 91-94° (0.36 g). The yield of bromo compound melting over a three degree range was equal to 63%.

After recrystallization from alcohol, 2-methyl-9-bromoanthracene formed yellow, transparent rhombic platelets with m.p. 94.5-95.5°.

4.979 mg substance: 12.106 mg CO_2; 1.757 mg H_2O. Found %: C 66.35; H 3.94. $C_{15}H_{11}Br$. Calculated %: C 66.42; H 4.09.

b) To a solution of phenyllithium(0.0058 mole) was introduced slowly 2 g 2-methyl-9,10-dibromoanthracene (m.p. 141-142° [11]). At the end of 30 minutes the organolithium compound was hydrolyzed with an ethereal solution of methanol, the reaction mixture was washed with water, the ether driven off and the residue (1.63 g) crystallized from alcohol. There was obtained 0.52 g substance with m.p. 82-87°; this was crystallized from 1:1 dioxane-alcohol to give 0.24 g with m.p. 93-95° and 0.12 g with m.p. 88-91° in the form of yellow platelets. Yield 24% of the theoretical. The melting point of a mixture of the compound melting at 93-95° with 2-methyl-9-bromoanthracene prepared by bromination of 2-methylanthracene was not depressed.

From the evaporated mother liquor, after separation of a fraction weighing 0.52 g, there was isolated 0.81 g of a low melting mixture of bromo compounds with m.p. 44-52°. Chromatography on alumina followed by crystallization from alcohol-ether gave a product with m.p. 43-53° which was found by analysis to be a mixture of the isomeric 2-methyl-9-bromo- and 2-methyl-10-bromoanthracenes.

6.077 mg substance: 14.764 mg CO_2; 2.148 mg H_2O. Found %: C 66.31; H 3.95. $C_{15}H_{11}Br$. Calculated %: C 66.42; H 4.09.

2,9-Dimethylanthracene. To an ethereal solution of phenyllithium (0.0037 mole) was added 1 g 2-methyl-9-bromoanthracene. At the end of 30 minutes addition was made of an ethereal solution of 1.58 g methyl iodide which reacted with the organolithium compound with considerable heat development. After holding for 30 minutes at room temperature, the reaction products were washed with water, the ether was driven off, and the residue (0.89 g) was crystallized from methanol.

There was obtained 0.28 g yellow crystalline substance with m.p. 81-82°; the mother liquor yielded a further 0.25 g with m.p. 79-82°. Yield 69.7% of the theoretical. The melting point of a mixture of the compound melting at 81-82° with 2,9-dimethylanthracene prepared by reacting 2-methyl-9-anthrone with methyl magnesium iodide [12] (m.p. 80.5-82°) was not depressed.

2-Methylanthracene-9-carboxylic acid. To a solution of n-butyllithium, prepared from 1.42 g n-butyl chloride, 0.21 g lithium and 30 ml ether, was added 2 g 2-methyl-9-bromoanthracene. After a period of 30 minutes the reaction mixture was carboxylated by pouring on to solid carbon dioxide. Crystallization of the acidic reaction products from dilute (50%) alcohol gave 10.5 g yellow crystals with m.p. 187-189°. Further crystallization of the acid from benzene gave 0.9 g substance with m.p. 197-198° in the form of light-yellow needlets. Yield equal to 51.7% of the theoretical.

4.825 g substance: 14.424 mg CO_2; 2.216 mg H_2O. Found %: C 81.58; H 5.13. $C_{16}H_{12}O_2$. Calculated %: C 81.33; H 5.12.

Judging by the melting point, the acid of unestablished structure (m.p. 197°) obtained by Liebermann [11, 13] by the action of oxalyl chloride on 2-methylanthracene is 2-methylanthracene-9-carboxylic acid.

2-Methyl-10-bromoanthracene-9-carboxylic acid. To a suspension (cooled to 0°) of 0.9 g 2-methylanthracene-9-carboxylic acid in 15 ml carbon bisulfide was slowly added, with stirring, a solution of 0.63 g bromine in 10 ml carbon bisulfide. When all the bromine had been added, the reaction mixture (a brown suspension) was heated on the water bath until hydrogen bromide ceased to come off; the solvent was then distilled off and the residue crystallized from dilute alcohol.

There was obtained 0.86 g substance with m.p. 205-213° (with decomp.). Crystallization from benzene gave 0.6 g (50% of the theoretical yield) of acid with m.p. 223.5-225° in the form of yellow needles. One more crystallization from benzene gave a melting point of 229-230.5°. A mixture of the acid with 2-methyl-9-bromoanthracene-10-carboxylic acid of m.p. 235-238°, prepared from 2-methyl-9,10-dibromoanthracene, melted at 217-233°.

5.505 mg substance: 12.205 mg CO_2; 1.734 mg H_2O. Found %: C 60.71; H 3.52. $C_{16}H_{11}O_2Br$. Calculated %: C 60.95; H 3.52.

Oxidation of 2-methyl-10-bromoanthracene-9-carboxylic acid. To a solution of 0.2 g 2-methyl-10-bromoanthracene-9-carboxylic acid in acetic acid, heated on the water bath, was added an acetic acid solution of 0.17 g chromic oxide. The reaction mixture was left for 18 hours at room temperature, after which the acetic acid was distilled off, and the residue was washed with water and crystallized from alcohol. There was obtained 0.08 g nearly colorless, slender needles (57% of theory) with m.p. 163-167°.

The melting point rose to 171-174° after crystallization from dilute acetic acid, and there was no depression of melting point in admixture with a specimen of 2-methylanthraquinone (m.p. 173-174°).

2-Methyl-9-bromoanthracene-10-carboxylic acid. To a solution of 3 g 2-methyl-9,10-dibromoanthracene in 20 ml absolute benzene was added an ethereal solution (11.8 ml) of 0.729 g phenyllithium. After the lapse of 30 minutes the reaction mixture was carboxylated by pouring on to solid carbon dioxide.

The acidic reaction product (2.68 g with m.p. 216-221°) was crystallized from dilute (50%) alcohol to give 1.59 g acid in the form of yellow needlets with m.p. 235-238° (with decomp.). Yield equal to 59% of the theoretical.

4.510 mg substance: 10.054 mg CO_2: 1.516 mg H_2O. Found %: C 60.84; H 3.76. $C_{16}H_{11}O_2Br$. Calculated %: C 60.95; H 3.52.

SUMMARY

1. The hydrogen atom in position 9 is substituted by bromine when one equivalent of bromine acts on 2-methylanthracene.

2. One equivalent of phenyllithium reacts with 2-methyl-9,10-dibromoanthracene with substitution of a halogen by lithium, preferentially in the 10-position.

3. Organic compounds of alkali metals are nucleophilic reagents.

4. In organometallic compounds of an alkali metal present in the ortho-position to the electronegative substituent, a bond is developed between the metal and the heteroatom which is similar in character to the hydrogen bond. This bond is the factor governing the orientation during metalation.

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SYNTHESIS OF THE SIMPLEST CYANINES

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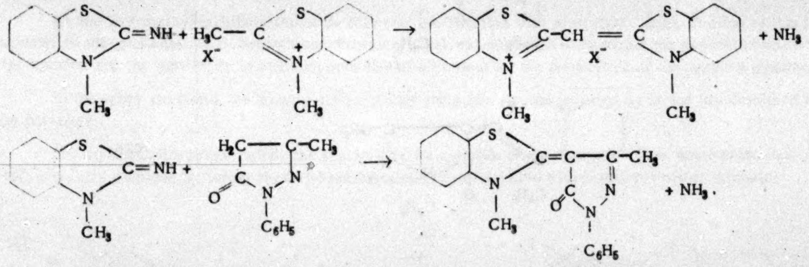
G. M. Oksengendler and A. I. Kiprianov recently showed [1] that auramine and the methylmethosulfate of Michler's thioketone are more susceptible to condensations with compounds containing active methyl or methylene groups than is Michler's ketone itself.

If we compare the derivatives of Michler's ketone, each with a carbonyl group, with the same derivatives of N-methylbenzothiazole, we can detect a profound similarity in their structure and properties. Thus, to Michler's ketone corresponds N-alkylbenzothiazolone; as we know, the latter compound is incapable of entering into a condensation reaction and Michler's ketone condenses with difficulty. To Michler's thioketone corresponds N-methylbenzothiazolonethione. Both compounds are nonreactive; however, the products of addition of dimethyl sulfate to these substances (the methylmethosulfate of Michler's thioketone and the methylmethosulfate of 2-methylmercaptobenzothiazole) are extremely reactive compounds. Finally, to auramine corresponds N-methylbenzothiazoloneimine.

On the basis of this analogy we suggested, and then demonstrated experimentally, that N-alkylbenzothiazoloneimines are also capable of condensing with heterocyclic compounds containing active methyl or methylene groups.

By short-period heating to 180-190° of heterocyclic bases with quaternary salts we have prepared monomethinecyanines, while with substances containing the $-CH_2-CO-$group (of the type of methylphenylpyrazolone) we prepared merocyanines (without a polymethine chain). The reactions proceed according to the equations:



The yield of monomethinecyanines is 60-70% of the theoretical, and that of merocyanines is 80-90%. These reactions do not take place in solvents (acetic anhydride, pyridine).

Merocyanines can also be obtained with N-ethyl-2-pyridonimine, but in low yield.

Several methods are now known for the preparation of monomethinecyanines and merocyanines (without a polymethine chain). The most widely applied of these is based on the reactivity of alkyl- or arylmercapto groups situated in the α- or γ-position to the quaternary heterocyclic nitrogen.

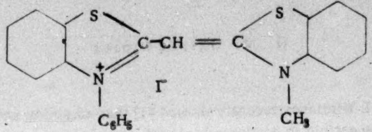
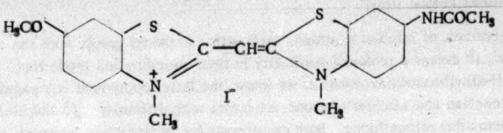
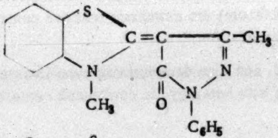
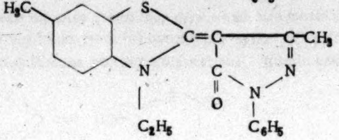
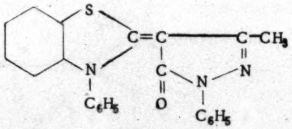
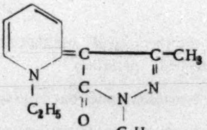
Other methods, based on utilization of quaternary salts containing a reactive iodine atom or a cyano group, have limited applicability.

The method of preparation of monomethinecyanines with the help of amyl nitrite in acetic anhydride may be adapted to reactions with an active cyano group.

The first method of preparation of monomethinecyanines reported in the literature — condensation of quinone- and quinaldine-alkyl iodides in presence of potassium hydroxide — is today of limited use.

The methods proposed by us for preparation of monomethinecyanines and merocyanines offer definite

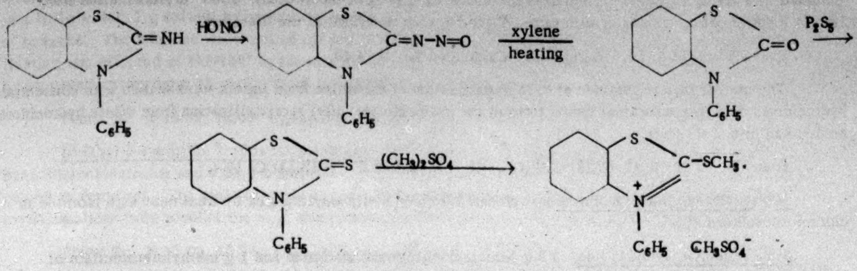
TABLE

Preparation No.	Formula	Melting point (corr)
(I)		278°
(II)		290
(III)		177
(IV)		143
(V)		280
(VI)		185

advantages over known methods of synthesis of these dyes if we exclude the simplest compounds prepared from 2-mercaptobenzothiazole. Actually, derivatives of 2-benzothiazoloneimine are more accessible compounds than the quaternary salts of the corresponding 2-alkylmercapto derivatives usually employed for the synthesis of dyes.

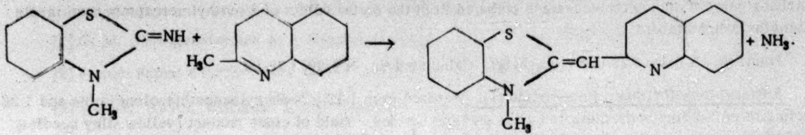
Thus, thiocyanation of p-anisidine readily yields 2-amino-6-methoxybenzothiazole, from which is obtained the N-alkyl-6-methoxybenzothiazoloneimines, whereas 2-mercapto-6-methoxybenzothiazole can only be prepared from the corresponding o-aminothiophenol by the action of carbon bisulfide [2].

The synthesis of monomethinecyanines and merocyanines of the benzothiazole series, containing aryl groups at the heterocyclic nitrogen, requires salts of 3-aryl-2-methylmercaptobenzothiazolium. These can be prepared only from the corresponding imines according to the scheme [3]:



If, however, we make direct use of N-arylbenzothiazoloneimines for the preparation of dyes, then four stages can be omitted. From N-phenylbenzothiazoloneimine we have prepared monomethinecyanine in 60% of the theoretical yield and merocyanine in 90% of the theoretical yield.

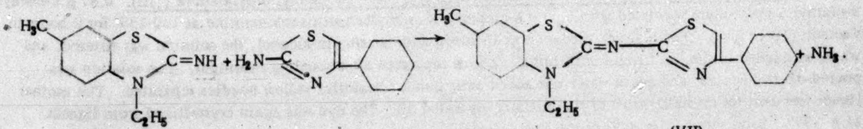
We only found one reference in the literature to a similar condensation. In 1936 Clark [4] prepared the base of pseudothiacyanine by condensation of N-methylbenzothiazoloneimine with quinaldine:



α- and β-2-methylnaphthothiazoles do not enter into reaction with α-picoline. Being limited to this sole example of the condensation of benzothiazoloneimine, Clark was unable to demonstrate the general character of this reaction and the possibility of utilizing benzothiazoloneimines for the preparation of the simplest cyanines.

In the table are listed the monomethinecyanines and merocyanines prepared by us and not described in the literature.

N-Alkylbenzothiazoloneimines can also be used for synthesis of azacyanines. Thus, azacyanine base (VII) is readily prepared by fusing N-ethyl-6-methylbenzothiazoloneimine with 2-amino-4-phenylthiazole.



(VII)

EXPERIMENTAL

2-Amino-4-phenylthiazole is prepared from acetophenone and thiourea with addition of bromine [5].

2-Amino-6-methoxybenzothiazole is prepared by thiocyanation of p-anisidine [6].

6-Methyl-N-ethylbenzothiazoloneimine is prepared from 2-amino-6-methylbenzothiazole by heating with ethyl iodide and subsequent treatment with caustic alkali [7].

N-Methylbenzothiazoloneimine. 1.5 g 2-aminobenzothiazole and 1.9 g methyl ester of p-toluenesulfonic acid were fused over a bare flame until a homogeneous melt was obtained, and then heated for 20 minutes at 140-150°. The reaction product was dissolved in 20 ml water (the whole dissolved) and into the still-warm solution was run, gradually, while rubbing with a glass rod, a solution of 1.3 g potassium hydroxide in 5 ml water. The imine came down in the form of lustrous crystals. On the following day the crystals were drained, washed with cold water and dried. Yield 1.2 g (73% of the theoretical); m.p. 124°. Hunter [8] gives m.p. 123°.

6-Methoxy-N-methylbenzothiazoloneimine. Prepared from 1.8 g 2-amino-6-methoxybenzothiazole and 2 g methyl ester of p-toluenesulfonic acid by the preceding procedure. The oily layer which separated on addition of the alkali was twice extracted with hot benzene, the benzene was distilled off and the residue of benzene was removed in a drying cupboard. Yield of crude imine 1.5 g (77% of theoretical). After crystallization from ligroin it forms colorless needles with m.p. 94° (corr.). Not described in the literature.

Found %: N 14.3, 14.4. $C_9H_{10}ON_2S$. Calculated %: N 14.43.

The mother liquors obtained after recrystallization of the imine from ligroin were shaken with concentrated hydrochloric acid in a separating funnel to form the hydrochloride; after recrystallization from dilute hydrochloric acid it had m.p. 320° (corr.).

Found %: N 12.10. Cl 15.15. $C_9H_{11}ON_2SCl$. Calculated %: N 12.14; Cl 15.4.

N-phenylbenzothiazoloneimine was prepared from N,N'-diphenylthiourea by treatment with bromine in chloroform solution [8].

3,3'-Dimethylcyanine iodide. 0.5 g N-methylbenzothiazoloneimine and 1 g methylmethosulfate of 2-methylbenzothiazole were pulverized together and then fused in vacuum for 15 minutes at 180-190°. Toward the end of the reaction the melt began to foam and solidified. The reaction product was dissolved in 30 ml alcohol, water was added until turbid, and the hot solution was filtered. The filtrate was heated and 5 ml acetone was added, followed by a solution of potassium iodide (3 g) in water (10 ml); the precipitated dye was filtered, washed with acetone, water, and again acetone. Yield of crude product (straw-colored silky needles) 0.86 g (66% of the theoretical). M.p.304° after recrystallization from alcohol; does not depress the melting point of monomethinecyanine prepared from the methoiodides of 2-methylmercaptobenzothiazole and 2-methylbenzothiazole.

Found %: N 6.24; I 29.02. $C_{17}H_{15}N_2S_2I$. Calculated %: N 6.39; I 28.99.

3-Phenyl-3-methylthiacyanine-iodide (I). Prepared from 1.13 g N-phenylbenzothiazoloneimine and 1.38 g methosulfate of 2-methylbenzothiazole by the previous method. Yield of crude product (yellow silky needles) 1.5 g (60% of the theoretical); recrystallization from alcohol gave 1.35 g with m.p. 278°.

Found %: I 25.32. $C_{22}H_{17}N_2S_2I$. Calculated %: I 25.40.

(6-Methoxy-3-methyl)-(6'-acetylamino-3'-methyl)-thiacyanine iodide (II). 0.4 g 6-methoxy-N-methylbenzothiazoloneimine and 0.66 g methylmethosulfate of 6-acetylaminobenzothiazole were fused and worked up as before. Yield of crude product 0.7 g (68% of the theoretical). Yellow crystalline powder, after recrystallization from alcohol; m.p. 290°.

Found %: N 8.0. $C_{20}H_{20}O_2N_3S_2I$. Calculated %: N 8.01.

4-[3'-Methyl-6'-methoxybenzothiazolinylidene-(2')]-[1-phenyl-3-methyl-5-pyrazolone] (III). 0.87 g 1-phenyl-3-methyl-5-pyrazolone was fused with 0.97 g 6-methoxy-N-methylbenzothiazoloneimine at 150-155° for 2 hours in vacuum (10-15 mm). The reaction product was dissolved with heating in alcohol, the solution was filtered, and water was added to the hot filtrate until turbid. An oil separated after standing overnight. The solution was poured off and heated, and again water was added until turbid. Beautiful yellow needles separated. The mother liquor was used for crystallization of the initially separated oil. The dye was again crystallized from ligroin M.p. 177°. Total yield 1.5 g (90% of the theoretical).

Found %: N 11.84, 11.74. $C_{19}H_{17}O_2N_3S$. Calculated %: N 11.96.

4-[3'-Ethyl-6-methylbenzothiazolinylidene-(2')]-[1-phenyl-3-methyl-5-pyrazolone] (IV). 0.87 g 1-phenyl-3-methyl-5-pyrazolone was fused with 0.96 g 6-methylbenzothiazoloneimine as in the preceding experiment, until ammonia ceased to come off. After recrystallization from aqueous alcohol, there was obtained 1.2 g (69% of the theoretical) of yellow prisms melting at 143°.

Found %: N 11.99, 11.85. $C_{20}H_{19}ON_3S$. Calculated %: N 12.03.

4-[3'-Phenylbenzothiazolinylidene-(2')]-[1-phenyl-3-methyl-5-pyrazolone] (V). Preparation as for (III), from 1.12 g N-phenylbenzothiazoloneimine and 0.88 g methylphenylpyrazolone. Fusion in vacuum was performed during 10 minutes at 170-180°. After crystallization from alcohol there was obtained 1.765 g (92% of the theoretical) of yellow needles. After recrystallization from toluene the m.p. was 280°.

Found %: N 10.87, 10.82. $C_{23}H_{17}ON_3S$. Calculated %: N 10.96.

4-[1'-Ethyldihydropyridylidene-(2')]-[1-phenyl-3-methyl-5-pyrazolone] (VI). 0.94 g 2-aminopyridine was fused with 2 g ethyl ester of p-toluenesulfonic acid at 130-140° for 20 minutes. The quaternary salt was dissolved in a little water, 1 g sodium hydroxide was added, and the pyridonimine three times extracted with small quantities of benzene. The benzene was distilled off and to the residual oil (0.9 g) was added 1.75 g methylphenylpyrazolone. Heating was effected at 150-160° in vacuum (30-40 mm) for 3 hours. Yellow needles with m.p. 185° were obtained by recrystallization from alcohol. Yield 0.14 g (5% of the theoretical).

Found %: N 14.88, 15.06. $C_{17}H_{17}ON_3$. Calculated %: N 15.05.

[3-Ethyl-6-methylbenzothiazolinylidene-(2)]-[2-amino-4-phenylthiazole] (VII). 0.96 g N-ethyl-6-methylbenzothiazoloneimine and 0.88 g 2-amino-4-phenylthiazole were fused at 165-170° in vacuum until ammonia ceased to come off. The yield of crude azacyanine base was 0.98 g (56% of the theoretical). After two crystallizations from alcohol the m.p. was constant at 186° (corr.). Nearly colorless, rhombic platelets.

Found %: N 12.00, 12.14. $C_{19}H_{17}N_3S_2$. Calculated %: N 11.94.

SUMMARY

1. A synthesis is proposed for the simplest cyanines, based on the ability of alkylbenzothiazoloneimines to enter into condensation with heterocyclic compounds containing an active methyl, methylene or amino group.

2. 7 dyes (the simplest cyanines) were synthesized by this method.

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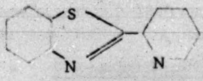
CONDENSATION OF o-AMINOTHIOPHENOL WITH HETEROCYCLIC CARBOXYLIC ACIDS

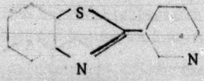
I. PYRIDYLBENZOTHIAZOLES

V. M. Zubarovsky and A. I. Voronina

The condensation of o-aminothiophenol with carboxylic acids of the heterocyclic series has not been investigated. This reaction can serve as a method of synthesis of benzothiazole derivatives containing various heterocycles in the 2-position; benzothiazoles of this type have not been investigated; a few of them are known. We have performed the condensation of o-aminothiophenol with the monobasic pyridine-carboxylic acids: picolinic, nicotinic and isonicotinic. The following isomeric pyridylbenzothiazoles were isolated: 2-[pyridyl-(α)]-benzothiazole (I), 2-[pyridyl-(β)]-benzothiazole (II), and 2-[pyridyl-(γ)]-benzothiazole (III).



(I)



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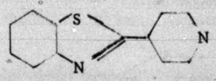
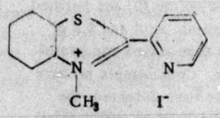


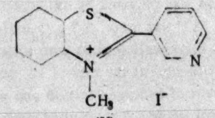
(III)

Condensation of o-aminothiophenol with the pyridinecarboxylic acids was effected by the usual method: heating of equimolar amounts of the starting components in sealed glass tubes. The condensation reaction is accompanied by a decarboxylation of the pyridinecarboxylic acids, and this is apparently the cause of the low yields (33-35%) of pyridylbenzothiazoles (I) and (II) obtained from picolinic and nicotinic acids. An attempt to replace nicotinic acid by its ethyl ester was unsuccessful, for the ester did not react with o-aminothiophenol after heating for 5 hours at 200°. The pyridylbenzothiazoles (I) and (II) are formed with higher yield (60%) by reacting o-aminothiophenol with the chlorides of picolinic and nicotinic acids. In the conditions of condensation with o-aminothiophenol, isonicotinic acid is less easily decarboxylated and 2-[pyridyl-(γ)]-benzothiazole is therefore obtained in a yield of 65%.

The isomeric pyridylbenzothiazoles possess basic character to extents depending on the mode of addition of the pyridine to the benzothiazole residue. Interest is attached to the mutual influence of these residues. 2-[Pyridyl-(α)]-benzothiazole is a very weak base: in dilute hydrochloric acid it does not dissolve without heating; in concentrated acid it dissolves in the cold but the salt formed in solution slowly hydrolyzes when excess of water is added; this pyridylbenzothiazole does not react with alkyl halides. One of its quaternary salts, 3-methyl-2-[pyridyl-(α)]-benzothiazole iodide (IV), was prepared by the action of the picolinic acid halide on o-methylaminothiophenol.



(IV)



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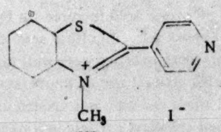
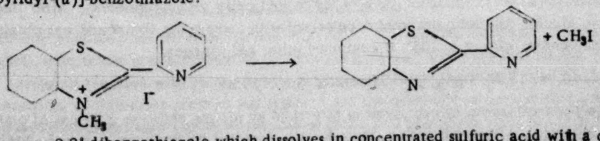


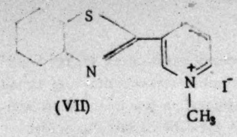
(VI)

This quaternary salt decomposes, however, when heated and is quantitatively transformed into methyl iodide and 2-[pyridyl-(α)]-benzothiazole:

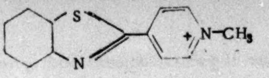


In contrast to 2,2'-dibenzothiazole which dissolves in concentrated sulfuric acid with a characteristic intense yellow color [1], 2-[pyridyl-(α)]-benzothiazole dissolves with a very weak yellow color. With divalent iron, 2-[pyridyl-(α)]-benzothiazole, like 2-[pyridyl-(α)]-quinoline [2], does not form a colored complex cation;

in this respect both of these compounds differ markedly from α,α'-dipyridyl, although their structures are similar. 2-[Pyridyl-(β)]-benzothiazole dissolves in concentrated sulfuric acid to form a nearly colorless solution. 2-[Pyridyl-(α)]-benzothiazole, on the other hand, is a fairly strong base; it dissolves in dilute hydrochloric acid with evolution of heat and forms a stable salt which can be isolated. It forms quaternary salts with alkyl halides. Analysis of these salts shows that 2-[pyridyl-(β)]-benzothiazole is a monoacidic base; salt formation proceeds at the expense of the pyridine residue, since it forms the compound (VII) with methyl iodide and this compound is not identical with the 3-methyl-2-[pyridyl-(β)]-benzothiazolium iodide (V) synthesized from o-methylaminothiophenol and nicotinic acid halide.

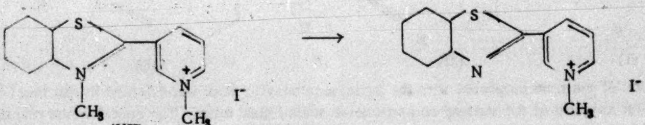


(VII)



(VIII)

The basic properties of the pyridine residue are so weakened in 3-methyl-2-[pyridyl-(β)]-benzothiazolium iodide that this compound does not react when heated with excess of methyl iodide. Heating to the melting point leads to isomerization:



(VII)

3-Ethyl-2-[pyridyl-(β)]-benzothiazolium iodide is also isomerized by the same method.

2-Pyridyl-(γ)]-benzothiazole unexpectedly proved to be closer in basic properties to 2-[pyridyl-(β)]-benzothiazole than to 2-[pyridyl-(α)]-benzothiazole. Qualitative tests indicate the 2-[pyridyl-(γ)]-benzothiazole is a somewhat weaker base than 2-[pyridyl-(β)]-benzothiazole, at least in relation to dilute hydrochloric acid; regarding the reactions with alkyl halides, both of these bases behave very similarly. 2-[Pyridyl-(γ)]-3-methylbenzothiazolium iodide (VI), in complete analogy with the above-described case, isomerizes when heated to form the methyl iodide of γ-[benzothiazolyl-(2)]-pyridine (VIII). 3-Ethyl-2-[pyridyl-(γ)]-benzothiazolium iodide likewise isomerizes. 2-[Pyridyl-(γ)]-benzothiazole dissolves in concentrated sulfuric acid with a yellow color which is even weaker than that formed by 2-[pyridyl-(α)]-benzothiazole.

EXPERIMENTAL

I. 2-[Pyridyl-(α)]-benzothiazole

The picolinic acid required for the synthesis was prepared by oxidation of α-picoline [3] and purified through the copper salt. Picolinic acid with m.p. 137° was used. 3.7 g (1 mole) picolinic acid and 3.8 g (1 mole) o-aminothiophenol were well mixed in a thick-walled glass tube which was then sealed and heated for 6 hours with gradual rise of temperature from 140-200° at the rate of 10° per hour. Considerable pressure was released when the tube was opened and the odors of hydrogen sulfide and pyridine were detected; the tube contained colorless cyrstals in a transparent red liquid. The crystals were filtered, washed with a small quantity of alcohol, triturated with 10 ml aqueous sodium carbonate, and again filtered and washed with water. An additional crop of product was obtained from the oil by dilution with alcohol and water. There was obtained 2.1 g 2-[pyridyl-(α)]-benzothiazole (33% of the theoretically possible amount). After three crystallizations from alcohol (the solutions were decolorized with carbon) the compound was obtained in the form of colorless needles with m.p. 135°; it contained sulfur and nitrogen.

Found %: N 13.03, 13.22. $C_{12}H_8N_2S$. Calculated %: N 13.21.

2-[Pyridyl-(α)]-benzothiazole was obtained in 60% yield by mixing benzene solutions of o-aminothiophenol and picolinic acid chloride. After purification, the substance prepared by this route had m.p. 135°, and its mixture with the compound prepared as above had the same melting point. This procedure for synthesis of

2-[pyridyl-(α)]-benzothiazole was identical with that described below for 2-[pyridyl-(β)]-benzothiazole from the chloride of nicotinic acid (experiment III).

2-[Pyridyl-(α)]-benzothiazole does not dissolve in aqueous solutions of caustic alkalies. It does not dissolve in dilute hydrochloric acid at 20-30°, but it is slightly soluble in the hot acid. It dissolves in concentrated hydrochloric acid in the cold, but addition of excess water to the solution causes it to separate slowly unchanged. Mixing of 5% hot alcoholic solutions of equimolar amounts of picric acid and 2-[pyridyl-(α)]-benzothiazole results in formation of the picrate, which comes down on cooling. M.p. 140-141° after several recrystallizations from alcohol.

Found %: N 15.58, 15.64. $C_{18}H_{11}O_7N_5S$. Calculated %: N 15.87.

With excess of picric acid (3 moles per mole base)a picrate with the same melting point as that of the above compound, and identical with it, was obtained (m.p. of mixed sample 140°).

II. Alkyl halide compounds of 2-[pyridyl-(α)]-benzothiazole

A. Heating of 2-[pyridyl-(α)]-benzothiazole with alkyl halides. 0.2 g 2-[pyridyl-(α)]-benzothiazole and and excess (1 ml) of methyl iodide were heated in a sealed glass tube in boiling water for an hour. The tube was opened, the methyl iodide driven off, and the residue recrystallized from alcohol to give nearly colorless needles with m.p. 134°; the mixture with 2-[pyridyl-(α)]-benzothiazole melted at the same temperature. We got the same result by using ethyl iodide and heating for 5 hours.

B. 3-Methyl-2-[pyridyl-(α)]-benzothiazolium iodide. The preparation was carried out by the method proposed for quaternary salts of benzothiazole by A. I. Kiprianov and Z. N. Pazenko [4]. The starting material, N-methyl-o-aminothiophenol, was prepared likewise by the method of these authors [5]; picolinic acid chloride was prepared by heating the acid with thionyl chloride [6]. Benzene solutions of N-methyl-o-aminothiophenol (4.17 g, 1 mole) and picolinic acid chloride (4.25 g, 1 mole) were gradually mixed; the reaction was exothermic and a yellow viscous precipitate was formed. The mixture was digested for 30 minutes, the liquid was decanted from the solidified precipitate, and the latter was washed with ether and dissolved in 20 ml water with gentle heating. The solution was heated with carbon, filtered and mixed with hot potassium iodide solution (5 g in 5 ml water). The yellow crystalline precipitate was washed with a small amount of water and alcohol (weight of precipitate 4.6 g) and twice recrystallized from alcohol. Yellow crystals were obtained which decomposed violently at 180-182° with formation of a transparent brown liquid, solidifying when cooled.

Found %: I 35.90, 35.85. $C_{13}H_{11}N_2IS$. Calculated %: I 35.88.

0.6 g 3-methyl-2-[pyridyl-(α)]-benzothiazolium iodide was heated with excess of methyl iodide (1 ml) in a sealed glass tube in boiling water for 5 hours. The methyl iodide was driven off and the residual product, after one crystallization from alcohol, had decomp. temp. 180° and was unchanged starting material.

C. Decomposition of 3-methyl-2-[pyridyl-(α)]-benzothiazolium iodide by heating. 2 g 3-methyl-2-[pyridyl-(α)]-benzothiazolium iodide was heated in a small flask with an exit tube in a sulfuric acid bath. The substance decomposed to form a dark-brown liquid and gave off a vapor. The distillate proved to be methyl iodide (pyridine-methoiodide with m.p. 118-119°). As soon as the whole of the substance taken for the experiment had been converted into liquid, the heating was stopped, and the liquid in the flask solidified when cooled. The solid product was twice recrystallized from alcohol and then from petroleum ether to give colorless crystals with m.p. 134°; their mixture with authentic 2-[pyridyl-(α)]-benzothiazole (m.p. 135°) melted at 134°.

Found %: N 12.90, 12.98. $C_{12}H_8N_2S$. Calculated %: N 13.21.

The picrate of the base with m.p. 140° was prepared.

III. 2-[Pyridyl-(β)]-benzothiazole

The nicotinic acid used for the synthesis had m.p. 231°. The starting materials, nicotinic acid and o-aminothiophenol, were taken in equimolecular amounts (10 g each). The condensation was effected as in the case of the analogous reaction with picolinic acid (experiment I), but the sealed tube was heated at 230-235° for 4 hours; on opening, considerable pressure was released and the odors of hydrogen sulfide and pyridine were noticed. To the contents of the tube (colorless crystals in brown oil) was added ether (30 ml); the undissolved crystals were filtered, washed on the filter with ether and then treated twice with 10% aqueous sodium carbonate solution for removal of unreacted nicotinic acid. There was obtained 5.8 g 2-[pyridyl-(β)]-benzothiazole or 34% of the theoretical yield. Crystallization from alcohol (treatment with animal charcoal) gave colorless needles, m.p. 128-129°, odorless. The compound contains nitrogen and sulfur.

Found %: N 13.07, 13.15; C 68.19; H 3.80; $C_{12}H_8N_2S$. Calculated %: N 13.21; C 67.92; H 3.77.

2-[Pyridyl-(β)]-benzothiazole was prepared in higher yield by condensation of o-aminothiophenol with nicotinic acid chloride. 5.6 g (1 mole) chloride and 5.0 g (1 mole) o-aminothiophenol were dissolved in benzene (10 ml in each case). Into the o-aminothiophenol solution was gradually stirred the solution of the chloride; the reaction was exothermic and a yellow precipitate was formed. The suspension was heated by gentle boiling for 30 minutes, the precipitate was filtered off, washed with benzene, triturated in a mortar with 30 ml 20% aqueous sodium hydroxide, again filtered and washed with water. Yield 4.8 g (57.0% of the theoretical). The substance was identical (mixed melting test) with the above-described 2-[pyridyl-(β)]-benzothiazole.

The picrate of 2-[pyridyl-(β)]-benzothiazole was prepared by mixing hot alcoholic solutions of equimolar amounts of picric acid and the base. The picrate is highly soluble in many organic solvents; it melts at 194-195° (from acetone). Use of excess picric acid gave a picrate identical with the preceding one. 2-[Pyridyl-(β)]-benzothiazole dissolves in 15% hydrochloric acid with evolution of heat; the salt can be isolated by dissolving the base (2 g) in concentrated hydrochloric acid (3 ml), adding alcohol (8 ml), decolorizing the solution with carbon, running in ether (6 ml) and leaving to stand. The salt is recrystallized from a small amount of alcohol. M.p. 215°.

Found %: Cl 14.17, 14.21. $C_{12}H_9N_2ClS$. Calculated %: Cl 14.28.

IV. Alkyl halide compounds of 2-[pyridyl-(β)]-benzothiazole

A. Reaction of 2-[pyridyl-(β)]-benzothiazole with alkyl halides. 0.65 g (1 mole) 2-[pyridyl-(β)]-benzothiazole and 0.43 g (1 mole) methyl iodide were heated for 1 hour in a sealed tube in boiling water. The product of reaction was washed with ether. Yield of methoiodide 0.95 g. It was crystallized from alcohol. The mother liquors were heated with carbon to remove resinous impurities. The pure salt melts at 231-232°. An identical product is obtained when using excess of methyl iodide and heating for a longer period.

Found %: I 35.94 35.75. $C_{13}H_{11}N_2IS$. Calculated %: I 35.88.

The ethoiodide of 2-[pyridyl-(β)]-benzothiazole was prepared by the same method. Light-yellow needles with m.p. 223-224° (from alcohol).

Found %: I 34.55, 34.52. $C_{14}H_{13}N_2IS$. Calculated %: I 34.51.

B. 3-Methyl-2-[pyridyl-(β)]-benzothiazolium-iodide. Method of preparation as in experiment II B. 3.8 g (1 mole) nicotinic acid chloride and 3.7 g (1 mole) N-methyl-o-aminothiophenol were reacted. Yield of salt 5.3 g. The product (4.4 g) was dissolved in three times the quantity of hot water and the solution poured into hot water containing KI (2.8 g in 10 ml). The yellow precipitate was filtered, washed with water and recrystallized from 10 times the amount of water. Dense yellow needles were obtained, melting at 206-208° to a liquid which immediately afterwards solidifies and again melts at a higher temperature.

Found %: I 35.97, 35.86. $C_{13}H_{11}N_2IS$. Calculated %: I 35.88.

The starting components did not react when the prepared methoiodide (1.2 g) and excess of methyl iodide (3 ml) were heated for 2 hours in a sealed tube in boiling water.

C. Isomerization of 3-methyl-2-[pyridyl-(β)]-benzothiazolium iodide. 1 g 3-methyl-2-[pyridyl-(β)]-benzothiazolium iodide was heated in a test tube in a sulfuric acid bath; the thermometer was immersed in the substance. Melting occurs initially at 203°, but the liquid immediately solidifies. The temperature of the mass in the test tube was raised to 225°, and the test tube was then cooled. The contents, a light-yellow crystalline mass, weighed 0.96 g. The product of isomerization was recrystallized 3 times from alcohol (decolorization with animal charcoal). The light-yellow, finely crystalline product melted at 232°.

Found %: I 35.93, 36.01. $C_{13}H_{11}N_2IS$. Calculated %: I 35.88.

The mixture of the isomerization product with the methoiodide of 2-[pyridyl-(β)]-benzothiazole, prepared by heating the latter with methyl iodide (experiment IV A), melted at 231-232°.

V. 2-[Pyridyl-(γ)]-benzothiazole

Isonicotinic acid was prepared by oxidation of 4-ethylpyridine [7], which was synthesized from pyridine and acetic anhydride [8]; the isonicotinic acid had m.p. 313° in a sealed capillary. A mixture of equimolar amounts of isonicotinic acid (2.5 g) and o-aminothiophenol (2.5 g) was heated in a sealed glass tube for 4 hours at 210-240°. Slight pressure was released when the tube was opened and hydrogen sulfide was detected. The reaction product was treated with 10 ml 10% aqueous sodium carbonate, and then dissolved in dilute hydrochloric acid (1:1) by heating. The solution was decolorized with carbon and precipitated with 20% sodium hydroxide solution. The crude 2-[pyridyl-(γ)]-benzothiazole was obtained in a yield of 65% of the theoretically possible. Insoluble in water, readily soluble in the cold or when heated in the majority of organic solvents. It was purified by crystallization from a large volume of alcohol and then from petroleum ether. Colorless, crystalline scales, m.p. 136°, odorless.

Found %: N 12.91, 13.10. $C_{12}H_8N_2S$. Calculated %: N 13.21.

The picrate of the base was prepared in nearly quantitative yield by mixing hot alcoholic solutions of the base and picric acid; poorly soluble in hot water, crystallizes from a large volume of acetone with m.p. 237°.

VI. Alkyl halide compounds of 2-[pyridyl-(γ)]-benzothiazole

A. Reaction of 2-[pyridyl-(γ)]-benzothiazole with alkyl halides. 0.45 g 2-[pyridyl-(γ)]-benzothiazole and 1 ml methyl iodide were heated in a sealed tube in boiling water for 30 minutes. Acetone was added to the reaction product, and the precipitate was filtered and washed with acetone. The crude product (0.45 g) was recrystallized from alcohol. The pure methoiodide, forming golden, orange-yellow crystals, darkened at 240° and melted at 256°.

Found %: I 35.92, 35.95. $C_{13}H_{11}N_2IS$. Calculated %: I 35.88.

The ethoiodide was prepared by heating sealed tubes in boiling water for 1 hour; the same compound was obtained regardless of whether equimolar amounts of reactants were used or whether the ethyl iodide was in excess. It melted at 219-220°; it was crystallized first from alcohol and then from water.

Found %: I 34.40, 34.48. $C_{14}H_{13}N_2IS$. Calculated %: I 34.51.

B. 3-Methyl-2-[pyridyl-(γ)]-benzothiazolium iodide. This quaternary salt was synthesized from N-methyl-o-aminothiophenol and isonicotinic acid chloride by the same procedure as for the analogous salts described in experiments II B and V B. The crude salt-chloride was washed with benzene and ether and converted into the iodide; the latter, after crystallization from water (treatment with animal charcoal), formed yellow crystals which darkened at 195° and melted at 197° to a dark liquid; the latter changed into light crystals with m.p. 253°.

Found %: I 35.98, 36.02. $C_{13}H_{11}N_2IS$. Calculated %: I 35.88.

The starting salt remained unchanged when 3-methyl-2-[pyridyl-(γ)]-benzothiazolium iodide was heated for 5 hours with excess of methyl iodide at 100°.

C. Isomerization of 3-methyl-2-[pyridyl-(γ)]-benzothiazolium iodide. 0.6 g 3-methyl-2-[pyridyl-(γ)]-benzothiazolium iodide was subjected to thermal isomerization as described in experiment IV C. The fusion started at about 180°, and the liquid solidified almost immediately. Heating was stopped as soon as the temperature of the melt had reached 220°. The product of isomerization (weight 0.57 g) was twice recrystallized from alcohol to give golden-yellow (dark) needles with m.p. 256° (after darkening at 240°).

Found %: I 35.84, 35.96. $C_{13}H_{11}N_2IS$. Calculated %: I 35.88.

The mixture of the isomerization product with the methoiodide of 2-[pyridyl-(γ)]-benzothiazole, prepared by heating the latter with methyl iodide (experiment VI A), melts at 256°.

SUMMARY

1. The isomeric 2-[pyridyl-(α)]-, 2-[pyridyl-(β)]-, and 2-[pyridyl-(γ)]-benzothiazoles were synthesized. The synthesis of these benzothiazole derivatives was effected by condensation of o-aminothiophenol with the pyridinemonocarboxylic acids or their chlorides.

2. The quaternary salts of the 2-pyridylbenzothiazoles were prepared and it was established that: a) after introduction into the 2-position of the benzothiazole molecule of the pyridyl-(α)-, pyridyl-(β)- and pyridyl-(γ)-residues, no basic properties were detected in the benzothiazole; b) the basic properties of pyridine are sharply diminished by the introduction of the benzothiazolyl-(2)-residue in the α-position of its molecule; when the same residue is introduced into the β- or γ-position, the basic properties of the

pyridine are only slightly weakened, although they disappear if a salt is formed at the nitrogen of the benzothiazole residue.

3. Isomerization is observed of the alkyl iodide compounds of 2-[pyridyl-(β)]- and 2-[pyridyl-(γ)]-benzothiazoles in which the alkyl is at the nitrogen atom of the benzothiazole residue; when these quaternary salts are heated to fusion point, the alkyl migrates to the nitrogen atom of the pyridine residue. The methoiodide of 2-[pyridyl-(α)]-benzothiazole decomposes when melted and evolves methyl iodide to leave the corresponding base.

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* See Consultants Bureau translation, p. 1515.

** See Consultants Bureau translation, p. 29.

REDUCTION OF DIOXINDOLE AT THE DROPPING MERCURY ELECTRODE

I. A. Korshunov and L. N. Sazanova

In a study of the reduction of isatin at the dropping mercury electrode* it was established that isatin belongs to the group of organic substances which undergo reduction at the dropping mercury electrode. Diffusion currents of isatin can be detected when the media are electrolytes with neutral, acid or alkaline reaction. In these solutions isatin is transformed in suitable conditions into isatinic acid with cleavage of the pyrrole ring. The speed of conversion depends on the pH of the solution and on the temperature, and it increases with rising pH and temperature of solution.

The structure of dioxindole is similar to that of isatin, so that we should expect it also to undergo reduction at the dropping mercury electrode with development of diffusion waves. The following experiments confirm the correctness of this assumption.

The dioxindole required for the investigation was synthesized by us by Heller's method: reduction of isatin with zinc dust in glacial acetic acid at room temperature. The dioxindole was extracted with hot alcohol and purified by repeated crystallization. The m.p. of the synthesized product was 178-180°. The investigation was carried out with an alcoholic solution of dioxindole containing 80% ethyl alcohol. Prior to the polarographic measurements the starting solution was mixed with the required solution of the medium in the proportion which gave the required concentration. Buffered and nonbuffered solutions were used as solutions of indifferent electrolytes. Buffered solutions were prepared from solutions of boric, acetic and phosphoric acids, neutralized with sodium hydroxide solution.

The unbuffered solutions were 1 N solution of lithium chloride, 2 N solution of lithium nitrate, a mixture of 0.5 N ammonia solution and ammonium chloride, and 0.2 N potassium hydroxide solution.

The electrolytic cell and the dropping mercury electrode were of normal design. Measurements were performed with a capillary which delivered mercury at the rate of 1.38 mg / sec and the period of dropping was 3.8 sec. The evolved oxygen was not removed since dissolved oxygen did not interfere with the polarographic measurements of the fairly concentrated dioxindole solutions. All measurements were performed at a temperature of 20 ± 0.5° in a thermostat. The half-wave potential of dioxindole was measured in relation to the reference saturated calomel electrode whose potential was arbitrarily assumed to be zero.

Diffusion currents were measured with the help of a visual polarograph and a galvanometer with a sensitivity of $0.49 \cdot 10^{-9}$ A per scale division.

EXPERIMENTAL RESULTS AND THEIR EVALUATION

Dioxindole diffusion currents with horizontal portions at the start and finish of the polarization curve were observed in buffer solutions whose pH was less than 5.15-5.20. In buffer solutions whose pH was higher than 5.15-5.20, a precipitate came down and diffusion waves of the reduction are not formed (Figure 1). In Table 1 are presented results of measurements of the half-wave potentials of dioxindole and values of the diffusion currents of the latter when using buffered solutions of the composition indicated above as indifferent electrolytes.

It follows from the data of Table 1 that the half-wave potential of dioxindole in buffered solutions remains substantially constant with changing pH of the medium and changing concentration of the substance which is being reduced.

The reduction of dioxindole in presence of solutions of lithium chloride and nitrate, ammonia and caustic alkalies is accompanied by formation of one diffusion wave on the polarograms. The numerical values of the potentials and diffusion currents of dioxindole in a medium of unbuffered solutions are set out in Table 2.

A yellow precipitate is formed in potassium hydroxide solutions and the diffusion current of dioxindole could not be detected.

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* I. A. Korshunov and M. K. Shchennikova, J. Phys. Chem. USSR, 24, 813 (1950).

TABLE 1

Half-Wave Potential and Diffusion Currents of Dioxindole in Buffer Solutions

pH value	$\pi^{1/2}$ (in V)		i_d (in μA)	
	Conc. of dioxindole (in mmol/l)		Conc. of dioxindole (in mmol/l)	
	1.9	3.5	1.9	3.5
1.03	1.06	1.06	4.35	8.84
2.50	1.05	1.05	4.54	8.80
3.25	1.04	1.06	4.56	8.80
3.76	1.06	1.04	4.54	8.43
4.17	1.07	1.07	4.47	8.43
4.76	1.06	1.04	4.54	8.23
5.15	1.06	1.04	4.54	8.43

TABLE 2

Half-Wave Potentials and Diffusion Currents of Dioxindole in a Medium of Unbuffered Solutions. Concentration of Dioxindole 1.9 mmol/l

Comp. of medium	$\pi^{1/2}$ (in V)	i_d (in μA)
1 N lithium chloride	1.06	3.92
1 N lithium nitrate	1.02	3.92
0.5 N ammonium chloride and 0.5 N ammonia	1.32	4.92
0.2 N potassium hydroxide	No wave	No wave

In the reduction of dioxindole at the dropping mercury electrode in an acid medium, a direct proportionality was observed between the diffusion current and the concentration; the following relation was valid between the current (in microamperes) and the dioxindole content (in millimoles per liter) for our capillary:

$$i_d = 2.46\ C,$$

where i_d is the diffusion current and C is the dioxindole concentration.

The straight-line plot for dioxindole in presence of a buffered solution of pH = 2.5 is given in Figure 2.

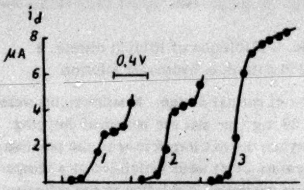

Fig. 1. Diffusion currents of dioxindole solutions in a medium of a buffer solution with pH = 2.5. 1) Concentration 1.1 mmol/l; 2) concentration 1.9 mmol/l; 3) concentration 3.8 mmol/l.

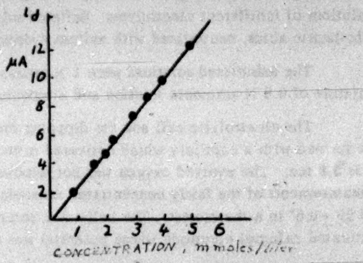

Fig. 2. Straight-line plot for dioxindole in a buffered solution with pH = 2.5.

The Ilkovic equation may be utilized for determination of the number of electrons participating in the reduction reaction:

$$i_d = 605\ nD^{1/2} n^{2/3}\ t^{1/6} C.$$

The diffusion coefficient of dioxindole, D, enters into this equation. We arbitrarily assumed the latter to be $0.3 \cdot 10^{-5}$ $c^2 sec^-$, no literature data being available.

On substituting our data and the above magnitude of the diffusion coefficient we obtain a value close to 2 for n, which indicates the two-electrode process of the reduction.

The Heyrovsky-Ilkovic equation for the polarographic wave can also be applied to the determination of the number of electrons participating in the reduction reaction of the dioxindole molecule:

$$\pi = \pi_{1/2} + \frac{2.3RT}{nF}\ \log \frac{i_d - i}{i}.$$

This equation is in good agreement with the experimental data for the dependence of the diffusion current on the potential of the dropping mercury electrode. All the experimental points lie on a straight line; however, the slope of the straight line in the π versus log $\frac{i_d - i}{i}$ plot gives value less than unity for n. The fractional value of n is probably due to the irreversibility of the process of reduction and the complexity of the reaction at the electrode.

SUMMARY

1. It is shown that the dioxindole molecule is reduced at the dropping mercury electrode in media with an acidic reaction.

2. The number of electrons participating in the reduction reaction of the dioxindole molecule is found.

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ISOQUINOLINE COMPOUNDS

VII. SYNTHESIS OF β-(α'-DIETHYLACETAL)-PROPYLGLUTARIC ACID

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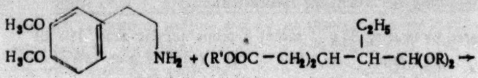
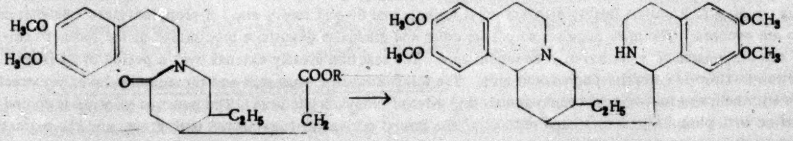
K. K. Kuzmina and N.A. Preobrazhensky

We have already drawn attention [1] to the importance in work on the synthesis of the alkaloid, emetime, of the investigation of compounds with a carbon skeleton corresponding to the central portion of the molecule of the alkaloid. The following compounds were previously prepared for this purpose: a) Ethyl ester of β-(α'-cyano)-propylglutaric acid; b) γ-ethyl-δ-valerolactone-β-acetic acid; and c) ethyl ester of β-(α'-bromometho)-propylglutaric acid [2]. In addition we have now developed a method for preparation of β-(α'-diethylacetal)-propylglutaric acid (I). By condensing this acetal with homoveratrylamine (II) we synthesized the ester of N-homoveratryl-δ-ethyl-α-piperidone-γ-acetic acid (III), which we previously described [2] and which leads to emetine (IV) through a series of steps:



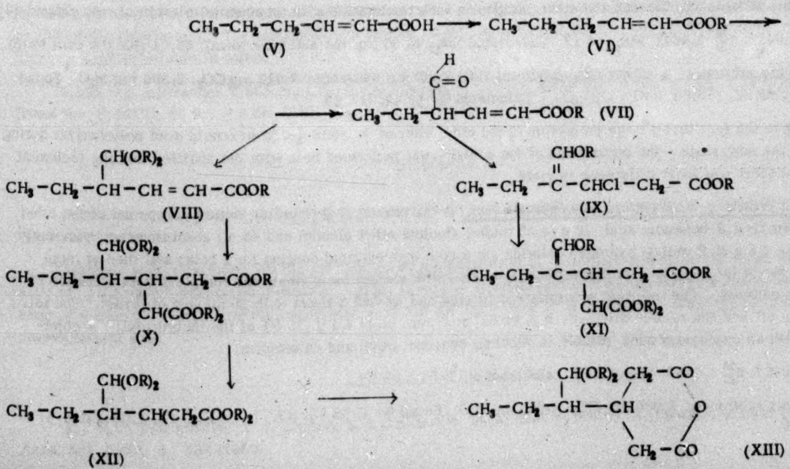
(II) (I)

$(R'OOC-CH_2)_2CH-CH(C_2H_5)-CH(OR)_2$



(III) (IV)

We effected the synthesis of β-(α'-diethylacetal)-propylglutaric acid (I, R' = H) by the following scheme.



(V) (VI) (VII) (VIII) (IX) (X) (XI) (XII) (XIII) β-Propylacrylic acid (V), prepared from butyraldehyde and malonic acid [3], is esterified to (VI) which is then condensed with ethyl formate to give the formyl derivative of the ester of β-propylacrylic acid [4] (VII). Heating of the ester of γ-formyl-α,β-hexenoic acid (VII) with ethyl orthoformate in a medium of alcohol in presence of a small amount of ammonium chloride as catalyst gives the ester of the acetal of γ-formyl-α,β-hexenoic acid [5] (VIII). On the other hand, reaction of the ester (VII) with alcohol in a current of dry hydrogen chloride gives the partial acetal, and a molecule of hydrogen chloride adds on at the double bond [6] (IX).

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* Deceased

Great difficulties are encountered in working with both the formyl derivatives and the acetals of the ester of hexenoic acid. Like other acrylic acid derivatives, these compounds rapidly polymerize. The pure compounds could be isolated by distilling them in a current of inert gas and in presence of a small amount of hexamethylene tetramine as stabilizer. Condensation of the ester of both of the acetals of γ-formyl-α,β-hexenoic acid (VIII and IX) with ethyl malonate in presence of sodium alcoholate leads to the corresponding tricarboxylic esters (X and XI). Saponification of the ester of α-carbethoxy-β-(α'-diethylacetal)-propylglutaric acid (X) with the calculated amount of an aqueous alcoholic solution of potassium hydroxide followed by acidification and decarboxylation results in separation of β-(α'-diethylacetal)-propylglutaric acid (XII), distillation of which in vacuum leads to the anhydride of the acid (XIII).

EXPERIMENTAL

β-Propylacrylic acid (V) is prepared by the usual method, e.g., by heating a stirred mixture of 60 g (1 mole) freshly distilled butyraldehyde (b.p. 75°), 87 g (1 mole) malonic acid, 40 ml pyridine and a few drops piperidine for 3 hours at 60-70° and for the same period at 110°. The pyridine is removed and the residue distilled in vacuum.

β-Propylacrylic acid is a white crystalline substance, highly soluble in alcohol and ethers, poorly soluble in cold water. B.p. 98-102° at 8 mm[2]; m.p. 34-35°. Yield 75 g, or 79% of the theoretical.

Ethyl ester of β-propylacrylic acid (VI) is prepared by heating 85 g (1 mole) β-propylacrylic acid, 120 ml absolute ethyl alcohol and 12 ml sulfuric acid (sp.g. 1.84) for 7 hours. B.p. 174-175° [2]. Yield 81 g or 76% of the theoretical. Colorless liquid, soluble in benzene, ether, alcohol and chloroform, insoluble in water.

Ethyl ester of γ-formyl-α,β-hexenoic acid (VII). Into 13 g (1 g-atom) metallic sodium in 400 g absolute toluene is run 50 g (1.2 moles) freshly distilled ethyl formate and 80 g (1 mole) ethyl β-propylacrylate. Bubbles of hydrogen are evolved. The mass acquires an orange color and gradually deposits a precipitate of the sodium compound of the ethyl ester of γ-formyl-α,β-hexenoic acid. The reaction usually extends over a period of 24 hours. The reaction mixture is carefully poured onto ice. The toluene layer is separated and the aqueous layer is extracted 3-4 times with benzene for removal of unreacted ethyl ester of propylacrylic acid. The aqueous solution is cooled and acidified with phosphoric acid (Congo red test). The formyl derivative is extracted with ether, and the extract is dried with sodium sulfate. Distillation of the solvent leaves 52 g (54 %) of technical ester of γ-formyl-α,β-hexenoic acid. From 10 g of the substance distilled at 65-70° (1 mm) in a nitrogen stream in presence of a small amount of hexamethylenetetramine was obtained 2.9 g ethyl ester of γ-formyl-α,β-hexenoic acid. Colorless liquid, soluble in benzene, alcohol and ether. It gives a violet coloration with an aqueous solution of iron chloride[3].

d_{20}^{20} 1.0412; n_D^{20} 1.4648; MR_D 45.17. Calculated MR_D 44.96 (for the aldehyde form), 46.01 (for the enol form).

3.005 mg substance 7.020 mg CO_2; 2.320 ml H_2O. 2.995 mg substance: 7.010 mg CO_2; 2.360 mg H_2O. Found %: C 63.70; 63.82; H 8.63, 8.81. $C_9H_{14}O_3$. Calculated %: 63.48; H 8.29.

Owing to the fact that a large proportion of the ethyl ester of γ-formyl-α,β-hexenoic acid polymerizes during distillation, the next stage – the preparation of the acetal – was performed both with the distilled and the technical material, but there was little difference in yield.

Ethyl β-chloro-γ-ethoxymethylenecaproate (IX). A mixture of 11 g (1 mole) sodium compound of the ethyl ester of γ-formyl-α,β-hexenoic acid, 12 g (4.55 moles) absolute ethyl alcohol and 45 ml absolute ether, previously saturated with 4.6 g (2.2 moles) hydrogen chloride are mixed with external cooling for 2 hours and then at room temperature for 14 hours. The reaction mixture is treated with sodium bicarbonate for complete neutralization of the hydrogen chloride. The resultant precipitate is filtered and washed 3 times with 15 ml lots of ether. The solvent is driven off and the residue distilled: b.p. 68-78° at 5 mm; yield 4.1 g (30.5% of the theoretical). A colorless liquid with an unpleasant odor, soluble in alcohol, benzene, ether and chloroform.

d_{20}^{20} 0.9927; n_D^{20} 1.4459; MR_D 62.98, calculated 60.70.

2.935 mg substance: 5.980 mg CO_2; 2.040 mg H_2O. Found %: C 55.56; H 7.77. $C_{11}H_{19}O_3Cl$. Calculated %: 56.25; H 8.16.

Ethyl ester of γ-(α'-diethylacetal)-α,β-hexenoic acid (VIII). To a mixture of 5 g (1 mole) distilled ethyl ester of γ-formyl-α,β-hexenoic acid and 4.35 g (1 mole) freshly distilled ethyl orthoformate is added 0.1 g (0.63 mole) ammonium chloride in 2 ml absolute alcohol. The mixture is then heated on a boiling water bath for 30 minutes. On the following day the liquid is decanted off, mixed with double the quantity of ether and washed several times with 5% ammonia solution until the turbidity disappears, and then with water until neutral. The ethereal solution is dried with potassium carbonate. The residue after removal of the solvent is distilled in vacuum in a nitrogen stream in presence of hexamethylenetetramine; b.p. 79-83° at 0.8 mm. Yield 2.55 g, or 35.6% of the theoretical. The ester is a colorless liquid, soluble in alcohol, ether and chloroform; insoluble in water.

3.135 mg substance: 7.325 mg CO_2; 2.650 mg H_2O. Found %: C 63.71; H 9.46. $C_{13}H_{24}O_4$. Calculated %: C 63.88; H 9.90.

Ethyl α-carbethoxy-β-(α'-ethoxymethylene)-propylglutarate (XI). To sodium alcoholate prepared from 4 ml absolute alcohol and 0.22 g (1 mole) metallic sodium is added at 30-40° 3 g (2 moles) ethyl malonate and the mixture kept at this temperature for 30 minutes. Addition is then made of 2 g (1 mole) ethyl ester of β-chloro-γ-ethoxymethylenecaproic acid. The mixture is heated for 5 hours. On the following day the alcohol is distilled off and the residue poured on to ice. The separated oil is extracted with benzene and the extract is dried with calcined sodium sulfate. The residue after removal of the benzene is distilled with addition of hexamethylenetetramine; b.p. 148-149° at 2.5 mm. Yield 1.7 g or 55.7 % of the theoretical. The ester is a colorless liquid, soluble in alcohol and ether, insoluble in water.

3.260 mg substance: 7.190 mg CO_2; 2.510 mg H_2O. 2.920 mg substance: 6.470 mg CO_2; 2.290 mg H_2O. Found %: C 60.14, 60.42; H 8.61, 8.77. $C_{18}H_{30}O_7$. Calculated %: C 60.29; H 8.44.

Ethyl ester of α-carbethoxy-β-(α'-diethylacetal)-propylglutaric acid (X). To sodium alcoholate prepared from 0.6 g(1 g-atom) sodium and 10 ml absolute alcohol is added 7.8 g (2 moles) ethyl malonate and 6 g (1 mole) ethyl ester of γ-(2'-diethylacetal)-α,β-hexenoic acid. The mixture is heated on a boiling water bath for 5 hours. The ethyl ester of α-carbethoxy-β-(α'-diethylacetal)-propylglutaric acid is separated by the usual method. B.p. 160-163° (1 mm). Yield 4.8 g or 48.3% of the theoretical. Colorless liquid, soluble in ether, alcohol and benzene, insoluble in water.

3.175 mg substance: 6.910 mg CO_2; 2.485 mg H_2O. 3.055 mg substance: 6.655 mg CO_2; 2400 mg H_2O. Found %: C 59.34, 59.40; H 8.75, 8.79. $C_{20}H_{36}O_8$. Calculated %: C 59.36; H 8.97.

β-(α'-Diethylacetal)-propylglutaric anhydride (XIII). To 5.5 g (1 mole) ethyl ester of α-carbethoxy-β-(α'-diethylacetal)-propylglutaric acid is added a solution of 4.6 g (6 moles) potassium hydroxide in 45 ml water and 45 ml methyl alcohol, and the mixture is refluxed for 5 hours. After distilling off the alcohol, the aqueous solution (cooled to 0°) of the potassium salt of the ethyl ester of α-carbethoxy-β-(α'-diethylacetal)-propylglutaric acid is mixed with 150 ml ether and carefully treated with hydrochloric acid until weakly acid. The ether layer is separated. Free acid is extracted from the aqueous solution with ether. After distilling off the solvent, the residue is heated on an oil bath for an hour at 160° (20 mm), after which it is distilled: b.p. 155-157° (4mm). Yield 1.3 g or 37% of the theoretical. The anhydride is a viscous liquid, darkening in the air, soluble in benzene, ether and alcohol; slightly soluble in water.

3.005 mg substance: 6.695 mg CO_2; 2.295 mg H_2O. 2.980 mg substance: 6.655 mg CO_2; 2.265 mg H_2O. Found %: C 60.75, 60.90; H 8.54, 8.50. $C_{13}H_{22}O_5$. Calculated %: C 60.43; H 8.59.

SUMMARY

1. Syntheses were effected of β-(α'-diethylacetal)-propylglutaric acid and its anhydride, intermediates for the synthesis of emetine.

2. Methods were developed for the preparation of the ethyl ester of γ-formyl-α,β-hexenoic acid and the ethyl ester of γ-(α'-diethylacetal)-α,β-hexenoic acid, as well as of substances confirming their structure: the ethyl ester of β-chloro-γ-ethoxymethylenecaproic acid and the ethyl ester of α-carbethoxy-β-(α'-ethoxymethylene)-propylglutaric acid.

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* See Consultants Bureau translation, p. 1931.

ISOQUINOLINE COMPOUNDS

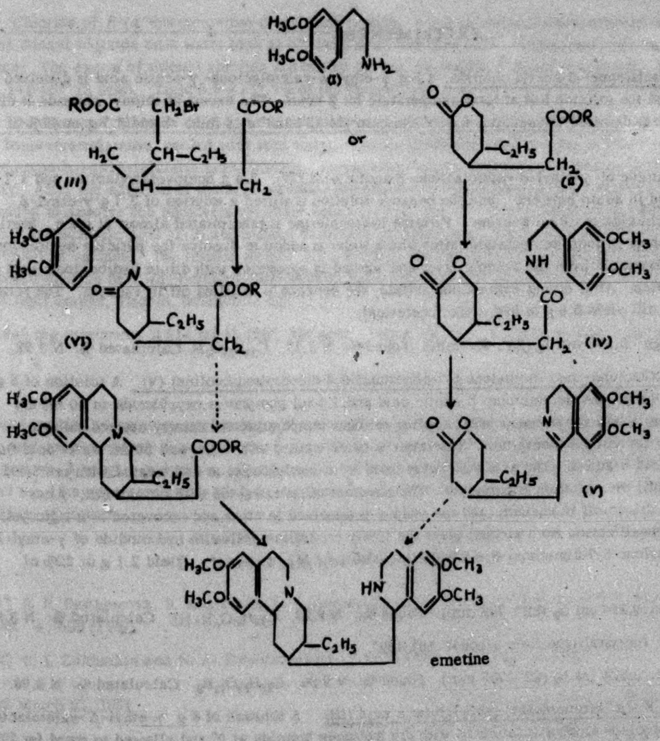
VIII. CONDENSATION OF α'-SUBSTITUTED β-PROPYLGLUTARIC ACIDS WITH HOMOVERATRYLAMINE

L. I. Zakharkin and N. A. Preobrazhensky

The basis of our synthesis of the alkaloid emetine [1] is the condensation of esters of α'-substituted β-propylglutaric acids with homoveratrylamine. We had earlier described the reaction between homoveratrylamine and the ester of β-(α'-cyano)-propylglutaric acid which successfully led through a series of intermediate compounds to the preparation of emetine.

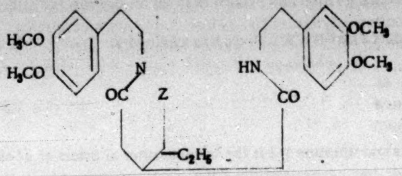
In this paper we describe the condensation of homoveratrylamine (1) with γ-ethyl-δ-valerolactone-γ-acetic acid (II) and β-(α'-bromometho)-propylglutaric acid (III), previously prepared by another route [2].

These syntheses are characterized by the following general scheme:



H_3CO
H_3CO
NH_2
(I)
ROOC
CH_2Br
COOR
H_2C
$CH—C_2H_5$
(III)
CH
CH_2
or
COOR
C_2H_5
CH_2
(II)
H_3CO
H_3CO
COOR
C_2H_5
(VI)
CH_2
NH
OCH_3
OCH_3
CO
C_2H_5
CH_2
(IV)
H_3CO
H_3CO
COOR
C_2H_5
N
OCH_3
OCH_3
C_2H_5
(V)
H_3CO
H_3CO
N
HN
OCH_3
OCH_3
C_2H_5
emetine

Reaction of starting compounds (II) and (III) with one molecule of homoveratrylamine (I) gives, respectively, the homoveratrylamide of γ-ethyl-δ-valerolactone-β-acetic acid (IV) [which is transformed with phosphorous oxychloride into the 6,7-dimethoxy derivative of dihydroisoquinoline (V)] and the ester of N-homoveratryl-δ-ethyl-α-piperidon-γ-acetic acid (VI). By performing this reaction with excess of homoveratrylamine we can isolate the diamides of structure (VII).



(VII)

the dihomoveratrylamide of β-(α'-oxymetho)-propylglutaric acid (when Z = CH_2OH) and the dihomoveratrylamide of β-(α'-bromometho)-propylglutaric acid (when Z = CH_2Br).

As we have previously shown [1], compounds (IV to VII) are intermediates for the synthesis of emetine. For example, cyclization of compounds (VII) followed by reduction leads to emetine; moreover, compounds (V) and (VI) can be utilized for elucidation of the stereochemical structure and of the effect of individual elements in the molecule on the physiological action of this alkaloid.

EXPERIMENTAL

1. γ-Ethyl-δ-valerolactone-β-acetyl chloride. 4.5 g γ-ethyl-δ-valerolactone-γ-acetic acid is dissolved in 5 ml thionyl chloride and the solution left at room temperature for 2 hours. The excess of thionyl chloride is distilled off and the residue is distilled in vacuum. B.p. of the chloride 137-138° at 3 mm. Yield 3.7 g or 47% of the theoretical.

2. Homoveratrylamide of γ-ethyl-δ-valerolactone-β-acetic acid (IV). 3.4 g homoveratrylamine and 1.7 g dry pyridine are dissolved in 50 ml benzene. Into the benzene solution is stirred a solution of 3.7 g γ-ethyl-δ valerolactone-β-acetyl chloride in 10 ml benzene. Pyridine hydrochloride is precipitated almost at once. Stirring is then continued for an hour at room temperature, after which water is added to dissolve the pyridine hydrochloride, the benzene solution is separated from the aqueous layer and washed in succession with dilute hydrochloric acid and sodium bicarbonate solution. After drying with sodium sulfate, the benzene is distilled off in vacuum. The residue is a light-brown, viscous oil; yield 5.6 g or 88% of the theoretical.

10.760 mg substance: 0.367 ml N_2 (23°, 728 mm). Found %: N 3.77. $C_{19}H_{27}O_5N$. Calculated %: N 3.92.

3. γ-Ethyl-δ-valerolactone-b-(1-methylene-6,7-dimethoxy-3,4-dihydroisoquinoline) (V). A solution of 5 g homoveratrylamide of γ-ethyl-δ-valerolactone-β-acetic acid and 7.5 ml phosphorus oxychloride in 50 ml dry toluene is heated at a gentle boil for an hour. After cooling to room temperature the faintly colored toluene solution is decanted from the viscous precipitate. The latter is twice washed with ether and 30 ml water acidified with 2 ml hydrochloric acid is added. The acid solution is freed from insoluble resins and treated with saturated sodium iodide solution until precipitation is complete. The resultant oil is extracted with chloroform. After drying, the chloroform is driven off in vacuum, and the residue is dissolved in ether and recovered as a light yellow amorphous powder. Recrystallization from alcohol gives the finely crystalline yellowish hydroiodide of γ-ethyl-δ valerolactone-β-(1-methylene-6,7-dimethoxy-3,4-dihydroisoquinoline). M.p. 199-201°. Yield 2.1 g or 32% of the theoretical:

4.475 mg substance: 0.127 ml N_2 (22°, 756 mm). Found %: N 3.27. $C_{19}H_{21}O_4N \cdot HI$. Calculated %: N 3.05.

M.p. of the picrate, recrystallized from alcohol, 181-182°.

3.750 mg substance: 0.324 ml N_2 (22°, 756 mm). Found %: N 9.94. $C_{25}H_{29}O_{11}N_4$. Calculated %: N 9.98.

4. Diethyl ester of β-(α'-bromometho)-propylglutaric acid (III). A solution of 6 g γ-ethyl-δ-valerolactone-β-acetic acid in 50 ml absolute alcohol is saturated with dry hydrogen bromide at 0° and allowed to stand for 12 hours. The alcohol is distilled off in vacuum and the residue poured into cold water and extracted with benzene. The benzene solution is washed with a sodium bicarbonate solution. The benzene is taken off in vacuum and the

ester is distilled at 140-141° (3 mm). Yield 7.5 g or 72% of the theoretical; n_D^{20} 1.4628.

3.020 mg substance: 5.325 mg CO_2; 1.945 mg H_2O. Found %: C 48.12; H 7.21 $C_{13}H_{23}O_4Br$. Calculated %: C 48.28; H 7.17.

5. Ethyl ester of N-homoveratryl- δ-ethyl- α-piperidon- γ-acetic acid (VI). A solution of 5 g diethyl ester of β-(α'-bromometho)-propylglutaric acid and 12 g homoveratrylamine in 30 ml dry toluene is heated on an oil bath at a gentle boil for $2\frac{1}{2}$ hours. After cooling, crystals of the hydrobromide are precipitated. Water is added and the toluene solution is separated from the aqueous layer and washed with dilute hydrochloric acid. The toluene is taken off in vacuum and the residue distilled. B. p. 227-231° (2 mm). Yield 1.3 g (21.6% of the theoretical).

3.105 mg substance: 7.645 mg CO_2; 2.195 mg H_2O. 3.010 mg substance: 7.410 mg CO_2; 2.250 mg H_2O. 5.169 mg substance: 0.171 ml N_2 (23°, 763 mm). Found %: C 67.19, 67.18; H 7.91, 8.36; N 3.83. $C_{21}H_{31}O_5N$. Calculated %: C 66.80; H 8.27; N 3.71.

6. Dihomoveratrylamide of β-(α-oxymetho)-propylglutaric acid (VII, Z = CH_2OH). 3 g γ-ethyl- δ valerolactone-β-acetic acid (III) is heated with 8 g homoveratrylamine for 4 hours at 190-200°. Water separates. After cooling, the light-brown mass is dissolved in benzene. The benzene solution is washed in succession with dilute hydrochloric acid and sodium carbonate solution. After drying with sodium sulfate, the benzene is taken off in vacuum; the residue weighs 5.8 g (68% of the theoretical). The product is a nonmobile oil, insoluble in ether.

3.280 mg substance: 7.845 mg CO_2; 2.365 mg H_2O. Found %: C 65.27; H 8.07. $C_{29}H_{42}O_7N_2$. Calculated %: C 65.61; H 7.98

7. Chloride of β-(α'-bromometho)-propylglutaric acid. 4 g β-(α'-bromometho)-propylglutaric acid is heated with 5 ml thionyl chloride on a water bath at 50° for 2 hours and then at the boiling point of the thionyl chloride for an hour. The excess of thionyl chloride is distilled off and the residue distilled in vacuum. B.p. of the acid chloride 141-143° (2 mm). Yield 3.5 g (77.5% of the theoretical).

8. Dihomoveratrylamide of β-(α'-bromometho)-propylglutaric acid (VII, Z = CH_2Br). To a benzene solution of 7.3 g homoveratrylamine, cooled with iced water, is added gradually, with stirring, a benzene solution of 3 g β-(α'-bromometho)-propylglutaric acid chloride. Homoveratrylamine hydrochloride begins to separate almost immediately. After the addition of the acid chloride, the mixture is stirred for $1\frac{1}{2}$ hours at room temperature. Water is then added to dissolve the homoveratrylamine hydrochloride, and the benzene solution is washed in succession with dilute hydrochloric acid (1:2) and sodium carbonate solution. After drying with sodium sulfate, the benzene is distilled off in vacuum. The residue weighs 4.9 g (83% of the theoretical). For the purpose of analysis the dihomoveratrylamide of β-(α'-bromometho)-propylglutaric acid was reprecipitated from alcohol by addition of ether. A light orange, viscous, nonmobile oil.

4.845 mg substance: 0.214 ml N_2 (22°, 740 mm). Found %: N 4.98. $C_{29}H_{41}O_6N_2Br$. Calculated %: N 4.72.

SUMMARY

Condensation of homoveratrylamine with γ-ethyl- δ-valerolactone-β-acetic acid or β-(α'-bromometho)-propylglutaric acid gave: γ-ethyl- δ-valerolactone-β-(1-methylene-6,7-dimethoxy-3,4-dihydroisoquinoline), the ester of N-homoveratyl- δ-ethyl-α-piperidon- γ-acetic acid, the dihomoveratrylamide of β-(α'-bromometho)-propylglutaric acid, and the dihomoveratrylamide of β-(α'-oxymetho)-propylglutaric acid – principal intermediate products in the synthesis of emetine.

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* See Consultants Bureau translation, p. 1931.

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THE ALKALOIDS OF OROBANCHE LUTEA

I. A NEW ALKALOID, OROBANCHAMINE

M. M. Rubinshtein*, G. P. Menshikov and P. S. Massagetov

The plant Orobanche lutea belongs to the Orobanchaceae family. It is a chlorophyll-free parasite which parasitizes the roots of plants. The material used in the present investigation was collected in the Transcaucasus. The pulverized above-ground parts of the plant were treated with ammonia solution and extracted with dichloroethane to yield a weak base in the pure, crystalline form. This product did not give an alkaline reaction to phenolphthalein. The alkaloid melts at 193-194° and has $[\alpha]_D$ +33.92°. The results of the elementary analyses given in the experimental part correspond most closely to the formula $C_{20}H_{31}O_{14}N$, but this formula cannot be considered final. With such a large molecular weight a change in formula by two hydrogen atoms only changes the content of the latter by 0.37 %, which is almost at the limit of analytical accuracy. Judging by the constants, but mainly by the empirical formula, the isolated alkaloid is a new, previously undescribed substance and we therefore propose the name of orobanchamine. The content of the alkaloid in the plant is very small: in the specimens that we investigated it did not exceed 0.06%, calculated on the air-dry material. The oxygen content is unusually high for an alkaloid and suggests the possibility of orobanchamine being a glucoalkaloid. Determination of the active hydrogen content by the Tserevitinov method, however, compels this supposition to be rejected.

EXPERIMENTAL

1.8 kg pulverized, air-dry above-ground parts of the plant were treated with 10% ammonia solution until a strong odor of ammonia persisted, and exhaustively extracted with dichloroethane. The dichloroethane extract was exhaustively extracted with 5% sulfuric acid solution. The acid solution was purified by shaking with ether, the ether was separated, and the acid solution was treated with excess of strong ammonia solution before being extracted with chloroform. The chloroform extract was dried with sodium sulfate, filtered, and the chloroform removed by distillation first at the ordinary pressure and toward the end in vacuum. There remained an oil which crystallized fairly quickly on standing. The crystalline mass was purified from the accompanying resins by trituration with 5 ml of a mixture of 2 parts chloroform and 1 part petroleum ether (b.p. 60-80°). After filtration and drying, the product weighed 1.1 g. It was recrystallized from 20 times the amount of the same mixture of chloroform and petroleum ether. After two recrystallizations it formed fine, colorless prisms melting at 193-194° and maintaining the same melting point after further recrystallizations.

0.0339 g subst.: 1 ml alcohol; 1 1 dm; α_D+1.15°; $[\alpha]_D$+33.92°. 4.567 mg subst.: 7.973 mg CO_2; 2.462 mg H_2O. 4.134 mg substance: 7.2[illegible] mg CO_2; 2.273 mg H_2O; 8.970 mg substance: 0.221 ml N_2 (23°, 736 mm). 7.210 mg substance: 0.183 ml N_2 (23°, 735 mm). Found %: C 47.61, 47.58; H 6.03, 6.13; N 2.75, 2.83. $C_{20}H_{31}O_{14}N$. Calculated %: C 47.13; H 6.13; N 2.75.

Sulfur and active hydrogen were not found.

Orobanchamine is readily soluble in alcohol, not so soluble in chloroform and ether, poorly soluble in water and petroleum ether.

SUMMARY

A new alkaloid of the composition $C_{20}H_{31}O_{14}N$, named orobanchamine, has been isolated from Orobanche lutea, a parasitic plant, and characterized.

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* Deceased.

INVESTIGATION OF THE ALKALOIDS OF *STIZOLOPHUS BALSAMITA* (LAM.)

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Stizolophus balsamita (Lam.) (*A. Takht.* = *Centaurea balsamita* Lam.) is an annual plant of the *Compositae* family. The above-ground portion consists of thin, rod-like branched stalks up to 80 cm in length. The leaves are lanceolate. The racemes are large, oviform panicles with yellow flowers. The plant is common in Transcaucasus, and in the Gruzian, Azerbaijan and Armenian SSR. The local population uses aqueous decoctions of stizolophus as a medicament, internally for fevers, externally as a gargle in tonsilitis and as a fomentation in shingles.

The material for study of the alkaloids and their pharmaceutical and anti-bacterial properties was gathered in 1948 during the phenophase of budding on June 27-28 on the dry slopes by the Riber Kura above the village of Aspindza and on July 19 during the climax of flowering in the plain to the east of the town of Tbilis where the plant is found in enormous quantities.

Extraction with dichloroethane of the ammonia-treated above-ground parts of the plant enabled us to isolate a crystalline, optically active ($[\alpha]_D$ + 24.6°) base which melted at 122-123° with decomposition. The analytical results point to the formula $C_{15}H_{23}NO_5$. Judging by the empirical formula and the constants, the base is a new compound, not previously described in the literature. We propose the name "stizolophine" for it.

The content of the alkaloid in the specimens of *Stizolophus balsamita* that we examined is about 0.3% *. The substance is readily soluble in alcohol and acetone, less soluble in water and chloroform. Aqueous solutions of the base (1 g in 100 g water) have a pH of 8.8. Solutions in dilute (5-10%) inorganic acids are unstable; on standing or on short-period heating, they develop a cherry-red color; we were unable to recover the unchanged base from these solutions. The majority of the salts of stizolophine that we prepared were amorphous; the only ones that crystallized were the salicylate $C_{15}H_{23}NO_5 \cdot C_7H_6O_3$, melting at 187-188°, and the viridiflorate** $C_{15}H_{23}NO_5 \cdot C_7H_{14}O_4$, m.p. 168-169°.

A biological study of stizolophine, carried out in the pharmacological department of the All-Union Research Institute of Pharmaceutical Chemistry by M. D. Mashkovsky and S. N. Milovanovaya, showed that the alkaloid possesses little activity pharmacologically and in respect of antibacterial action.

EXPERIMENTAL

4.6 kg air-dry, pulverized, above-ground parts of the plant were wetted with 10% ammonia solution and exhaustively extracted with dichloroethane. The dichloroethane extracts were shaken with 10% sulfuric acid solution used without excess in quantity sufficient for neutralization. The acid solution was treated, while cooling, with excess of 25% ammonia solution and extracted with chloroform. The chloroform extracts were dried with sodium sulfate before evaporation to a small volume. On cooling, stizolophine crystallized in the form of white needles which filled the whole of the liquid. Two crystallizations from chloroform gave 12 g white, very slender crystals, m.p. 122-123°.

3.470 mg substance: 7.728 mg CO_2; 2.482 mg H_2O. 3.871 mg substance: 8.648 mg CO_2; 2.724 mg H_2O. 3.173 mg substance: 6.997 mg CO_2; 2.201 mg H_2O. 4.985 mg substance: 10.990 mg CO_2; 3.401 mg H_2O. 7.920 mg substance: 0.327 ml N_2 (23.5°, 725 mm). 9.360 mg substance: 0.378 ml N_2 (23.0°, 734 mm). 6.130 mg substance: 0.255 ml N_2 (24.5°, 734 nm). 6.700 mg substance: 0.269 ml N_2 (22.5°, 733.5 mm). 4.864 mg substance: 5.47 ml $Na_2S_2O_3$. 0.0756 g substance: 41.31 g benzene: Δt 0.033°. Found %: C 60.74, 60.93, 60.14, 60.12; H 8.00, 7.87, 7.76, 7.63; N 4.55, 4.52, 4.60, 4.47; NCH_3 10.86; M 281. $C_{14}H_{20}O_5(NCH_3)$. Calculated %: C 60.59; H 7.80; N 4.71; NCH_3 9.75; M 297.

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* In addition to *Stizolophus balsamita* we investigated another two plants of the *Centaurea* family for their content of organic bases by the dichloroethane extraction method. *Centaurea macrocephala*, collected at the Sevansk Pass on July 10, 1948, contains 0.3% of total noncrystallizing bases (calculated on the dry plant); *Centaurea squarrosa*, collected in the Kura River valley above Akhaltsikh on July 24, 1948, contains a total of 0.12% of noncrystallizing bases.

** Viridifloric acid is prepared by saponification of the alkaloid viridiflorine [J. Gen. Chem., 18, 1736 (1948)].

Equivalent weight: 0.2072 g substance: in 20 ml water, 6.80 ml 0.1 N HCl (potentiometrically-inflection of curve at pH 5.35), equiv. wt. 304.

Specific rotation: 1,272 g substance in 10 ml water, $\underline{l} = 1$ dm; α +3.13°; $[\alpha]_D$ +24.6°.

Stizolophine salicylate was prepared by adding an alcoholic solution of salicylic acid to an alcoholic solution of the alkaloid until the reaction was acid to methyl orange. The salt crystallized on rubbing with a glass rod; m.p. 168-169° after recrystallization from acetone.

8.020 mg substance: 0.260 ml N_2 (22.0°, 734 mm). 8.795 mg substance: 0.270 ml N_2 (21.5°, 734 mm). Found %: N 3.62, 3.44 $C_{15}H_{23}NC_5 \cdot C_7H_6O_3$. Calculated %: N 3.21.

Stizolophine viridiflorate was prepared by mixing acetone solutions of the base and viridifloric acid. The salt came down on standing and melted at 168-169° after crystallization from acetone.

8.060 mg substance: 0.228 ml N_2 (26.0°, 732.0 mm). 7.895 mg substance: 0.226 ml N_2 (27.0°, 732.0 mm). Found %: N 3.10, 3.13. $C_{15}H_{23}NO_5 \cdot C_7H_{14}O_4$. Calculated %: N 3.04.

SUMMARY

A new alkaloid, stizolophine $C_{15}H_{23}NO_5$, was isolated from Stizolophus balsamita (Lam.). The plant contains approximately 0.3% of the alkaloid.

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INVESTIGATION OF THE ALKALOIDS OF NARDOSMIA LAEVIGATA

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Nardosmia laevigata DC. is a perennial herbaceous plant belonging to the Compositae family.

Nardosmia is a diclinous plant, throwing out floriferous stalks with yellow clusters of flowers early in the spring shortly after the melting of the snow. The leaves develop after flowering. The leaf laminae are large (15 X 25 cm), reniform, broad-crenate, perfectly smooth, located at long petioles seated on the rhizomes. The rhizome is long and creeping; in the fresh state it has a characteristic odor. The plant grows at the bottom of swiftly flowing streams and in the water close to the banks of rivers, often forming dense beds of weeds. It is found in the Altai, in the North European part of the USSR, in the Urals and in Northern Mongolia. In the Altai the plant is considered to have medicinal value. A decoction of the leaves and roots is drunk in nervous ailments and as a sedative. For the study of the alkaloids, leaves of the plant were gathered on July 21-24 at the River Malaya Ulba (Western Altai).

Although studies of the alkaloids of Nardosmia laevigata are not reported in the literature, the fact that it belongs to the Compositae family suggests the possibility that they contain alkaloids of the heliotridane series which occur in various Senecio plants of the same family. This surmise has been fully confirmed and we have been able to isolate and identify the alkaloids of the plant with relative ease. We isolated the alkaloids by the usual method of extraction of the bases with dichloroethane from the ammonia -wetted plants. We succeeded in isolating three of the alkaloids present in the plant.

Alkaloid no. 1 is insoluble in water and boiling acetone. It was purified by crystallization from chloroform and then melted at 238°; it is levorotatory: $[\alpha]_D$ −61.5° ($CHCl_3$, c 3.087). The elementary analysis indicates the formula $C_{18}H_{25}O_5N$. A comparison of the empirical formula and constants of this base with those of the alkaloid senecionine [1] indicated the possibility that they were identical. For comparison we prepared the picrate and nitrate of the base and carried out the saponification of alkaloid no. 1, isolating and characterizing the acid and the base obtained. Table 1 sets out the constants of the prepared substances and those of senecionine, its salts and hydrolysis products [1-4,8], and leaves no doubt about the identity between alkaloid no. 1 and senecionine.

TABLE 1

	Alkaloid no. 1	Senecionine	Mixed sample
Base, m.p.	238°	232°	
$[\alpha]_D$	−61.5°	−56.67°	
Picrate, m.p.	193.5°	191°	
Nitrate, m.p.	214°	214°	
Base obtained after saponification of the alkaloid, m.p.	119−120°	121−122°	119−120°
$[\alpha]_D$	+56.9°	+53.29°	
hydrochloride of this base, m.p.	163−164°	163−164°	
Acid obtained after saponification of the alkaloid, m.p.	148−148.5°	151°	148−148.3°
lactone of this acid, m.p.	155−156°	155−156°	155−156°

Alkaloid no. 2 is insoluble in water and dissolves in boiling acetone. It was separated from alkaloid no. 1 by extraction with boiling acetone and was then purified through the bitartrate. After recrystallization from acetone the base had the composition $C_{18}H_{27}NO_5$ and melted at 127-129°. After crystallization from alcohol, the bitartrate of the base had mp. 198-199° and $[\alpha]_D$ − 37.6° (H_2O, c 2.099) the picrate melted at 197-198°. . The composition of the second alkaloid and the constants of the base and its salts agree with the data for the alkaloid platyphylline [4, 5,6] discovered by A. P. Orekhov. We confirmed the identity between these

TABLE 2

	Alkaloid no. 2	Platyphylline	Mixed sample
Base, m.p.	127−128°	129°	127−128°
Bitartrate, m.p.	198−199°	196°	198−199°
$[\alpha]_D$	−37.6°	−38.8°	−
Picrate, m.p.	197−198°	199 200°	198−199°

substances by the absence of depression of the melting point of a mixture of alkaloid No. 2 and platyphylline or of the melting point of a mixture of their bitartrates. Table 2 contains the constants of the bases and salts of alkaloid No. 2 and of platyphylline and the melting points of the mixed specimens.

Alkaloid no. 3 dissolves readily in water, which property permitted its separation from the first two alkaloids. The base was purified by crystallization from acetone, and it then melted at 193-195°. The bitartrate melted at 210° after crystallization from alcohol. A comparison of the constants of this alkaloid with those of renardine, first discovered by A. Danilova and R. Konovalova [7], suggested identity between these two compounds, and this was substantiated by the absence of depression in the mixed melting tests with the bases and their bitartrates. Comparative data appear in Table 3.

TABLE 3

	alkaloid no. 3	renardine	mixed specimen
Base, m.p.	193 – 195°	191 – 193°	193 – 195°
Bitartrate, m.p.	201°	198 – 198.5°	199°

EXPERIMENTAL*

Isolation of the alkaloids. 22 kg air-dry plant was wetted with 10% aqueous ammonia and exhaustively extracted with dichloroethane. The alkaloids were extracted from the dichloroethane extracts with 10% sulfuric acid solution. The acid extract was treated with aqueous ammonia which brought out the water-insoluble bases (43 g); the alkaline mother liquor was extracted with chloroform. The total amount of alkaloids (19 g) obtained after driving off the chloroform was again dissolved in 30 ml 10% sulfuric acid and the solution made alkaline with ammonia. The water-insoluble bases were separated (15 g) and the mother liquor was extracted with chloroform. Removal of the chloroform left 3 g of partly crystallizing bases, soluble in water.

Alkaloid no. 1. 58 g of the total bases insoluble in water was extracted with 300 ml acetone while boiling under a reflux condenser. The insoluble residue was separated from the hot acetone extract and then recrystallized from chloroform to give 25 g product melting at 238°.

0.3087 g substance in 10 ml $CHCl_3$, $\underline{1}$ = 1 dm, α −1.90°, $[\alpha]_D$ −61.5°. 2.905 mg substance: 6.776 mg CO_2; 1.874 mg H_2O. 3.190 mg substance: 7.421 mg CO_2; 2.086 mg H_2O. 8.480 mg substance: 0.348 ml N_2 (24.0°, 728.5 mm). 8.040 mg substance: 0.308 ml N_2 (22.5°, 731.5 mm). Found %: C 63.61, 63.45; H 7.22, 7;31; N 4.52, 4.25. $C_{18}H_{25}O_5N$. Calculated %: C 64.4, H 7.45; N 4.19.

The picrate was prepared from mixed alcoholic solutions of the base and picric acid melted at 191° (from alcohol). The nitrate was prepared by acidifying the alcoholic solution of the base with alcoholic nitric acid. The salt melted at 214° after crystallization from alcohol.

Saponification of the alkaloid. 1.3 g alkaloid, 3 g barium hydrate and 15 ml water were refluxed for 8 hours, after which carbon dioxide was passed through the solution, the barium carbonate was filtered off, and the mother liquor was made acid with hydrochloric acid and exhaustively extracted with ether. The ether extract was dried with sodium sulfate and the ether distilled off to leave 0.5 g white crystalline acid which after crystallization from 25 ml dry chloroform gave 0.4 g acid melting at 148-148.5°. A mixture with senecionic acid, prepared by us by saponification of platyphylline, melted at the same temperature.

The lactone was prepared by heating 0.5 g acid for 3 hours with 10% hydrochloric acid. The solution was extracted with ether. After drying with sodium sulfate the ether was evaporated to a small volume and 0.4 g substance came down; m.p. 155-156°. A mixture with the lactone of senecionic acid melted at 155-156°. After extraction with ether, the hydrochloric acid solution was evaporated to dryness in a beaker. The crystalline residue was extracted with absolute alcohol and the solution evaporated to a small volume. Addition of ether brought down 0.4 g crystalline hydrochloride of the base which melted at 163-164°.

A mixed sample with the hydrochloride of retronecine melted at the same temperature. The base was obtained by treating the aqueous solution of the hydrochloride with sodium hydroxide until alkaline to phenolphthalein, evaporating the solution to dryness, and extracting the residue with absolute alcohol. The residual crystalline base, following evaporation of the alcohol, melted at 119-120° after recrystallization from acetone. A mixed specimen with retronecine melted at the same temperature.

0.0172 g substance in 1 ml C_2H_5OH, $\underline{1}$ = 0.5 dm, α + 0.49°, $[\alpha]_D$ + 56.9°,

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* In collaboration with R. I. Bogomazova.

Alkaloid no. 2. The acetone extract after removal of the first alkaloid was evaporated to one quarter of its original volume. On cooling, it deposited 20 g base with m.p. 122-124°. The bitartrate of this base was prepared by adding a saturated alcoholic solution of tartaric acid to the alcoholic solution of the alkaloid until the reaction was acid to methyl orange. The precipitated salt melted at 198-199° after recrystallization from alcohol.

0.2099 g substance in 10 ml water, $\underline{l}$ = 1 dm, α −79°, $[\alpha]_D$ −37.6°.

The mixture with the bitartrate of platyphylline melted at 198-199°.

The base was obtained by dissolving the bitartrate of alkaloid no. 2 in water, treating the solution with aqueous ammonia, filtering the precipitate and recrystallizing from acetone. M.p. 127-128°. Mixture with platyphylline had same m.p.

3.960 mg substance: 9.250 mg CO_2; 2.927 mg H_2O. 4.070 mg substance: 9.494 mg CO_2; 3.040 mg H_2O. 9.135 mg substance: 0.346 ml N_2 (21.0, 732.5 mm). 9.155 mg substance: 0.350 ml N_2 (23.5°, 731.0 mm). Found %: C 63.71, 63.62; H 8.27, 8.35; N 4.24, 4.23. $C_{18}H_{27}NO_5$. Calculated %: C 64.1; H 8.01; N 4.17.

The picrate was prepared by mixing alcoholic solutions of the base and picric acid. After crystallization from alcohol, the salt melted at 197-198°. The mixture with platyphylline picrate melted at 198-199° (m.p. of platyphylline picrate 199-200°).

Alkaloid no. 3. 3 g of the total water-soluble bases was triturated with a small amount of acetone; the crystalline substance was filtered off and recrystallized from acetone and then melted at 193-195°. A mixture with renardine melted at the same temperature. The bitartrate was prepared by acidifying (methyl orange) an alcoholic solution of the alkaloid with an alcoholic solution of tartaric acid. M.p. (from alcohol) 201°. M.p. of mixture with renarcine bitartrate 199° (renardine bitartrate, prepared from *Senecio Renardi*, had m.p. 198-198.5°).

SUMMARY

Three alkaloids — senecionine, platyphylline, and renardine — were isolated from the plant *Nardosmia laevigata*.

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* See Consultants Bureau translation, p. 1989.

THE REACTION OF NICOTINE WITH METAL SALTS

I. REACTION OF NICOTINE WITH COBALT THIOCYANATE

S. E. Burkat

Little light is thrown in the literature on the reaction of nicotine with thiocyanates. A. A. Shmuk [1] mentions the precipitation of nicotine with solutions of potassium-platinum thiocyanate, zinc thiocyanate and calcium thiocyanate. The author did not state the composition and properties of the reaction products. In the present author's recent publication [2] it was shown that nicotine and its salts give in presence of ammonium thiocyanate readily crystallizing, characteristic precipitates with salts of nickel, cobalt, manganese and other metals. The composition and character of the obtained compounds were not established. In view of the general chemical interest of these compounds, we have made an investigation of their composition and of some of their properties.

Little attention has been given to the composition of the products of reaction of nicotine with salts of various metals. Nicotine is a strong organic base and when added to solutions of salts of heavy metals it precipitates their hydroxides [3]. Some of the qualitative reactions for nicotine are similar to those for pyridine, evidently due to the presence of the pyridine ring in the molecule [4]. It is known that pyridine in presence of ammonium thiocyanate forms with cadmium and copper salts complexes that are sparingly soluble in water [5]. We might assume nicotine would also form complex compounds in the same conditions. This property was indicated by A. A. Shmuk. The same author points out, however, that little attention has so far been given to the complex compounds of nicotine with bismuth, mercury and other metals. On the other hand, a number of authors describe the ease with which nicotine forms double salts with various metals [6,7]. In a number of cases nicotine yields compounds of variable composition with metal salts.

Our investigation of the preparation, composition and properties of compounds of nicotine with cobalt thiocyanate showed that addition of a solution of complex cobalt thiocyanate to an aqueous solution of nicotine or of its salts gives an amorphous precipitate with a light-to-dark-blue color, which rapidly changes into a pink, crystalline precipitate. The reaction product can be readily recrystallized from water at the boil.

The product has a sharp melting point (with partial decomposition), is sparingly soluble in cold water and more soluble on heating. It has slight solubility in ethyl alcohol in the cold and rather better solubility in hot alcohol, forming a dark-blue solution. It is not appreciably soluble in ether, chloroform, dichloroethane and benzene. With the help of common reagents the presence of ions of cobalt and thiocyanate and of nicotine was readily established in the saturated aqueous solution. The aqueous solution of the substance titrates with caustic alkali, indicating that nicotine is present in the form of a salt. Analyses revealed that the compositions of the compound prepared from nicotine base and from its salts were constant. All these facts point to the formation of a double salt of nicotine with Co thiocyanate and not of a complex compound.

EXPERIMENTAL

We isolated the nicotine for the investigation from technical nicotine sulfate by extraction with ethyl ether in presence of caustic alkali followed by steam-distillation. Nicotine was extracted from the aqueous solution with ethyl ether and the solvent was removed in the usual way.

Preparation of double salt of nicotine thiocyanate and cobalt thiocyanate. 2.25 g crystalline cobalt nitrate $Co(NO_3)_2 \cdot 6H_2O$ is dissolved in 5 ml water. In a separate vessel a solution is prepared of 5 g ammonium thiocyanate in 5 ml water and the two solutions are mixed. Into a 200 ml flask is introduced 2.5 g nicotine (base), 50 ml water is added and the liquid is neutralized with 25% hydrochloric acid (using methyl red as indicator). The solution of the cobalt thiocyanate complex is energetically stirred into the nicotine solution and the mixture is stood for 15 minutes. At first an amorphous light-to-dark-blue precipitate is formed which changes into a pink, crystalline one. This is drained and dried at room temperature. Yield of technical product 4.30 g or 90.3% of the theoretical if we assume that the compound is formed according to the following equation:

$$2C_{10}H_{14}N_2 \cdot HCl + Co(NO_3)_2 \cdot 6H_2O + 4NH_4CNS = (C_{10}H_{14}N_2)_2 \cdot 2HCNS \cdot Co(CNS)_2 + 6H_2O + 2NH_4NO_3 + 2NH_4Cl.$$

Melting point of the technical product 194-196°.

The technical product is dissolved in 60 ml water by boiling, and the solution is filtered without delay under reduced pressure. Rapid separation occurs of a dark-to-light-blue mass which quickly changes into pink crystals. After cooling to 15°, the crystals are drained on a Buchner funnel and again recrystallized from 40 ml water at the boil. The crystals are dried between sheets of filter paper at room temperature. Yield of pure product 2.20 g, m.p. 199-200°.

Subsequent experiments showed that: 1) The synthesis of the preparation is better performed with a solution of a nicotine salt since addition of the complex cobalt thiocyanate to the nicotine-base solution results in a pink, crystalline precipitate which contains light-to-dark-blue particles; the greater the dilution of the nicotine solution the lower the yield of reaction product; 3) with increasing acidity of the medium of the solutions, the yield of reaction product falls.

The prepared compound is a dark-pink crystalline substance. Solubility in water at 15° is 0.35%. Aqueous solutions are colored pink. The compound dissolves in normal inorganic acids, with difficulty in acetic acid. It dissolves without any special characteristics in concentrated sulfuric, nitric and hydrochloric acids. Precipitates characteristic of cobalt are formed when caustic alkali, ammonia and ammonium sulfate are added to the aqueous solution of the prepared compound. The reactions with potassium ferro- and ferricyanides are not quite typical of those for cobalt. Instead of the typical brownish-red precipitate given by cobalt with potassium ferrocyanide solution, there is formed a greenish precipitate which fairly quickly changes to dirty-blue. With potassium ferricyanide solution the aqueous solution of the compound gives a green precipitate.

With common alkaloid reagents the aqueous solution of the prepared compound gives the precipitates typical of alkaloids. Addition of iron chloride to the aqueous solution of the compound causes a blood-red coloration; addition of silver nitrate brings down silver thiocyanate.

Cobalt was quantitatively determined in the preparation by the gravimetric method in the form of sulfate. Nicotine was determined by steam distillation in presence of alkali and common salt, followed by titration with 0.1 N hydrochloric acid (methyl red as indicator). Quantitative determination of the thiocyanate ion was performed with a saturated aqueous solution of the compound by the argentometric method.

0.5000 g, 0.4860 g, 0.5050 g substance: 0.1320 g, 0.1214 g, 0.1280 g $CoSO_4$. 0.3124 g, 0.5000 g, 0.2560 g substance: 19.72 ml, 32.46 ml, 16.61 ml 0.1 N $AgNO_3$. 0.2388 g, 0.2522 g, 0.2500 g substance: 7.40 ml, 7.90 ml, 7.65 ml 0.1 N HCl. Found %: Co 10.02, 9.48, 9.62; CNS' 36.61, 37,65, 37.62; nicotine 50.33, 50.74, 49.57. $(C_{10}H_{14}N_2)_2 \cdot 2HCNS \cdot Co(CNS)_2$. Calculated %: Co 9.54; CNS' 37.64; nicotine 52.50.

Determination of the thiocyanic acid combined with the nicotine was performed by titration of the aqueous solution of the compound with 0.1 N sodium hydroxide in presence of phenolphthalein. Since the aqueous solution of the substance is colored pink, the volume taken for the titration is diluted with water until the color disappears.

0.3024 g, 0.2522 g, 0.1604 g substance: 9.60 ml, 7.90 ml, 5.10 ml, 0.1 N NaOH. Found %: HCNS 18.73, 18.47, 18.75. $(C_{10}H_{14}N_2)_2 \cdot 2HCNS \cdot Co(CNS)_2$. Calculated %: HCNS 19.13.

SUMMARY

The double salt of nicotine thiocyanate with cobalt thiocyanate was prepared. Its composition and properties have been studied and it has been shown to correspond to the formula $(C_{10}H_{14}N_2)_2 \cdot 2HCNS \cdot Co(CNS)_2$.

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PIRYLENE

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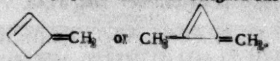
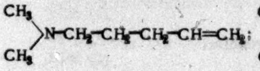
In 1888 a hydrocarbon of the composition C_8H_8 was first synthesized and given the name of "pirylene". Its structure has remained unestablished up to now. Originally it was assigned the structure of cyclopentadiene [1]. Later it was entered in the handbook literature as a hydrocarbon of the aliphatic series of unestablished structure [2]. Later, on the basis of a study of the molecular refraction, Braun and Teuffert [3] arrived at the conclusion that pirylene should be assigned one of the following two structures:



Oxidation of pirylene by these authors gave oxalic acid and acetic acid. In presence of palladium the hydrocarbon combined with 4 atoms of hydrogen. These data are inadequate for making a choice between the alternative structures. The authors refrained from selection of one of them.

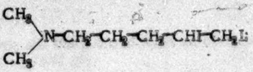
The starting material for the preparation of pirylene is piperidine. Exhaustive methylation of the latter gives des-N-dimethylpiperidine (I). Reaction of this with alcoholic iodine solution with iced-water cooling converts it quantitatively into the diiodo compound (II). Short-period heating of the latter with caustic alkali causes cleavage of one molecule of hydrogen iodide, and intramolecular rearrangement takes place to form a pyrrolidine derivative (III) whose structure has been fairly satisfactorily established [4,5,6]. Treatment of this compound with silver oxide leads to a free quaternary base which decomposes when heated and forms the so-called dimethylpiperideine whose structure was not established. Braun and Teuffert [3] suggest that this amine contains either a cumulated or an isolated system of double bonds, (IV, V). Dimethylpiperideine is unstable. It readily resinifies when kept. Its methoiodide decomposes when heated with caustic alkali and forms the hydrocarbon pirylene. It is interesting to note that the yield of hydrocarbon is negligible when the alkali is replaced by silver oxide.

CH



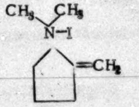
$(CH_3)_2N-CH_2-CH_2-CH_2-CH=CH_2$;

(I)

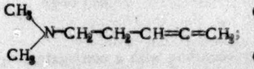


$(CH_3)_2N-CH_2-CH_2-CH_2-CHI-CH_2I$;

(II)

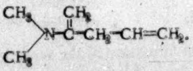


(III)



$(CH_3)_2N-CH_2-CH_2-CH=C=CH_2$;

(IV)



$(CH_3)_2N-\overset{CH_2}{\overset{\parallel}{C}}-CH_2-CH=CH_2$.

(V)

In the present investigation pirylene was synthesized in the precise conditions described in the literature [1,3,6]. The yields of the hydrocarbon and intermediate products agreed with those in the literature. The prepared hydrocarbon differed somewhat in physical properties from the hydrocarbon of Braun and Teuffert. M.p. 57-58°.

d_4^{20} 0.7412; n_D^{20} 1.45797; MR_D 24.29. C_8H_6 F F. Calculated: MR_D 22.82. Exaltation 1.47.

The hydrocarbon does not react with reagents for monosubstituted acetylenes. Hydrogenation over platinum black causes addition of 6 hydrogen atoms. Consequently, contrary to the statements of Braun and Teuffert, pirylene must contain either three double bonds (very improbable) or a double and a triple bond.

Raman spectra were plotted to assist in the elucidation of the structure.

$\Delta\nu$: 238 (3), 259 (3 w), 319 (3), 261 (2), 397 (2), 422 (2), 468 (5), 518 (5), 548 (2), 658 (2), 678 (1), 703 (2), 732 (2), 791 (1), 869 (1), 913 (1), 1029 (1), 1082 (8), 1106 (1), 1163 (10), 1276 (2), 1295 (6 w), 1380 (5), 1412 (8), 1559 (1), 1586 (1), 1609 (10), 1618 (5), 1936 (4), 2098 (1), 2137 (1), 2189 (4), 2237 (10), 2339 (1), 2860 (1), 2889 (1), 2921 (8), 2984 (4), 3013 (3), 3099 (2).

We see from the above data the the pirylene spectrum contains a series of frequencies both in the

1600 cm^{-1} region and in the 2200 cm^{-1} region. This confirms that pirylene contains both a double and a triple bond. The low value of the frequencies of the double bond (1609 and 1618 cm^{-1}) shows that the double bond is at the end of the hydrocarbon chain and is also conjugated.

The frequency of the triple bond (2237 cm^{-1}) shows that the acetylene is disubstituted.

On the basis of the foregoing data we can assign to pirylene the structure $CH_3-C\equiv C-CH=CH_2$.

This structure accords well with the above-mentioned oxidation products.

In this connection it was of interest to clarify the structure of dimethylpiperideine. Spectroscopic examination of this amine was made very difficult by the ease of resinification of the free amine and its high sensitivity to irradiation.

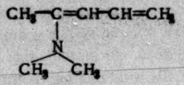
The freshly distilled amine had b.p. 73-75° (100 mm).

d_4^{20} 0.8024; n_D^{20} 1.4618; MR_D 38.01. $C_7H_{13}N\overline{|}_2$. Calculated: MR_D 37.53.

Raman spectrum of the amine: 290 (2), 341 (1), 855 (1), 909 (1), 962 (1), 1020 (1), 1049 (1), 1124 (3), 1191 (1), 1229 (3), 1266 (1), 1309 (3), 1374 (5), 1411 (2), 1439 (2), 1458 (4), 1504 (2), 1531 (3), 1596 (4), 1650 (20), 2232 (2), 2313 (1), 2491 (3), 2880 (2), 2921 (1), 2989 (1).

The spectrum contains frequencies of 1596 and 1650 cm^{-1}. The latter have an extraordinarily high intensity. This permits us to conclude that dimethylpiperideine contains a conjugated system of double bonds. Also the presence in the spectrum of the frequency 2232 cm^{-1} with a low intensity indicates that dimethylpiperideine is not a pure substance but is contaminated with a small amount of an amine containing a β-acetylenic bond. The amount of the latter may be estimated at 10-15%.

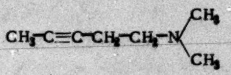
It follows from the spectroscopic data that the main component of dimethylpiperideine must be assigned the structure:



$$CH_3-\underset{\underset{CH_3\quad CH_3}{N}}{C}=CH-CH=CH_2$$

Exhaustive methylation of this amine should lead to formation of a hydrocarbon with a conjugated acetylenic-ethylenic bond.

The byproduct present in dimethylpiperideine must be assigned the structure:

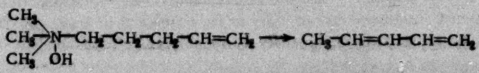


$$CH_3-C\equiv C-CH_2-CH_2-N\begin{matrix}CH_3\\CH_3\end{matrix}$$

Exhaustive methylation of this amine leads to formation of the same hydrocarbon with a conjugated acetylenic-ethylenic bond.

Consequently, the opening of the pyrrolidine ring (III) in the present case is accompanied by isomerization which leads to formation of a hydrocarbon with a conjugated system of bonds.

Isomerization during exhaustive methylation was observed for the first time in the classical synthesis of piperylene. In this case, instead of a hydrocarbon with isolated bonds, formation takes place of piperylene containing a conjugated system of bonds [7]



$$\begin{matrix}CH_3\\CH_3\\CH_3\end{matrix}\!>\!\underset{OH}{N}-CH_2-CH_2-CH_2-CH=CH_2 \longrightarrow CH_3-CH=CH-CH=CH_2$$

We prepared piperylene by exhaustive methylation of des-N-dimethylpiperidine. In the spectrum of this hydrocarbon the frequencies 1596 and 1645 cm^{-1} correspond to a conjugated system of double bonds. It was of interest to compare the frequencies of the conjugated bond system of this piperylene with the frequencies of the conjugated system of the same hydrocarbon prepared by other methods. In the preceding communication [8] we showed in collaboration with I. N. Shokhor that the spectrum of piperylene prepared by regeneration from its crystalline tetrabromide with m.p. 114.5° contains four double-bond frequencies: 1596, 1603, 1646 and 1655 cm^{-1}. The suggestion was made that these frequencies, taken in pairs, correspond to the cis-form (1596 and 1646 cm^{-1}) and the trans-form (1603 and 1655 cm^{-1}).

The same four frequencies were found in the spectrum of piperylene prepared from its liquid tetrabromide; however, two of them (1603 and 1655 cm^{-1}) were much more intense than the others. Bearing in mind that the trans-form must be characterized by higher frequency values than the cis-form, it had to be assumed that the trans-form predominates in piperylene prepared from the liquid tetrabromide. The data obtained in the present investigation show that exhaustive methylation of des-N-dimethylpiperidine gives exclusively cis-piperylene (frequencies of 1596 and 1645 cm^{-1}). The spectrum of the pure trans-piperylene might be expected to contain only the frequencies 1603 and 1655 cm^{-1}. This was confirmed by examination of piperylene prepared by cleavage of hydrogen chloride from α-chloroethylcyclopropane [8].

The table contains the data for the Raman spectra of the above four specimens of piperylene.

Raman Spectra of Piperylene Prepared			
by exhaustive methylation of des-N-dimethylpiperidine	from the crystalline tetrabromide	from the liquid tetrabromide	by cleavage of HCl from α-chloroethylcyclopropane
386 (5)	386 (5)	386 (5)	386 (3)
478 (2)	478 (5)	478 (5)	478 (4)
618 (1)			
	814 (1)	816 (1)	816 (5)
899 (2 w)	897 (4 w)	897 (3 w)	898 (4 w)
952 (2)	955 (1)	955 (1)	
1034 (1)	1032 (1)	1034 (1)	
1106 (0.5)			
1167 (3)	1174 (3)	1172 (3)	1174 (3)
	1183 (7)	1184 (6)	1188 (10)
1191 (1)			
1248 (10)	1250 (8)	1248 (6)	1248 (2 w)
1295 (8)	1292 (10)	1290 (10)	1292 (8)
		1324 (1)	
1388 (2)	1376 (6)	1376 (5)	1379 (2)
	1413 (5)	1413 (4)	1413 (2)
1435 (4)	1432 (3)	1434 (2)	1430 (5)
1468 (4)	1451 (6)	1451 (6)	1451 (5)
1596 (3)	1596 (4)	1596 (0)	
	1603 (4)	1602 (6)	1603 (1)
1645 (10)	1646 (10)	1646 (2)	
	1655 (10)	1655 (10)	1655 (10)

SUMMARY

1. Pirylene is 1-Penten-3-yne.

2. The main component is dimethylpiperideine is 4-dimethylamino-1,3-pentadiene. It contains an impurity in the shape of 1-dimethylamino-3-pentyne.

3. The hydrocarbon formed by the exhaustive methylation of des-N-dimethyl-piperidine is cis-piperylene.

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DISCUSSION

THE STATE OF THE THEORY OF CHEMICAL STRUCTURE IN ORGANIC CHEMISTRY

B. A. Kazansky and G. V. Bykov

The creative development of A. M. Butlerov's theory of chemical structure is the main task now confronting Russian chemists in the field of theory. Dialectical materialism—the methodological basis of Soviet science—requires the study of phenomena and their cause, movement and change. Consequently without an historical approach to the subject matter of the basic concepts and laws of the theory of chemical structure, it is impossible to detect the profound conceptual changes in them or the tendencies that are inherent in their development at the present day.

At the Conference on the Theory of Chemical Structure organized by the Division of Chemical Sciences of the Academy of Sciences in June, 1951, the idealistic theory of resonance or mesomerism was rightly subjected to annihilating criticism. There was thus removed a fundamental obstacle to the fruitful development of the theory of organic chemistry, a development that would be impossible without creative discussions, without the clash of ideas, without criticism and self-criticism. In order, however, that the creative discussions of our chemists should be fruitful, we must make a critical evaluation of the relevant problems without any polemic sophistics that would hinder the objective clarification of controversial topics.

We believe that in the first place we must exchange ideas on the following fundamental problems: 1) Modern ideas on chemical structure; and 2) the modern approach to the relation between properties and structure of organic compounds. As was revealed at the Conference on the Theory of Chemical Structure, there are many different, frequently incompatible, points of view in connection with each of these questions, and it is here that agreement between Soviet chemists is particularly necessary.

I

Scientific concepts change, being enriched by new content as science reflects more and more fully and accurately the field of objective reality that it explores. This implies that we must base the modern content of chemical structure on the history of our knowledge of the structure of molecules.

According to the theory of radicals—the first theory of organic chemistry—organic compounds consist of relatively autonomous parts (complex radicals). The various modifications of the theory of radicals, dualistic in principle, were more or less closely associated with the electrochemical hypothesis. All of them came into direct conflict with experiment and were abandoned in the fifties of last century. Dumas replaced them by his theory of types, according to which the substances possessing the same number and distribution of atoms belonged to one and the same mechanical type (mechanical system). At that time, of course, chemists could not visualize a spatial distribution of atoms, although many unfounded hypotheses were put forward, based mostly on crystallographic analogies and the study of specific volumes. A reaction to the current ideas was Gerhardt's declaration that chemical methods of investigation are inadequate for evaluation of the "molecular constitution of substances, i.e. the actual arrangement of their atoms". Gerhardt's types, unlike those of Dumas, were solely intended to express the reactivity of organic compounds. Berthollet proposed to characterize organic compounds by equations of formation (genetic equations), free from any hypotheses and simply expressing the facts. This was the standpoint of extreme empiricism and it erred in that chemical concepts and theory are able to reflect true actuality. This approach was only an attempt at systematization; the theory was judged solely from the standpoint of its expediency. Philosophical agnosticism was the methodological basis of this trend in chemistry.

The concepts of types had a positive value insofar as they led to two important generalizations to the concept of atomicity (valence) of elements or of a specific number of units of affinity; and, second, to the concept of the linking of atoms with one another through the "expenditure" (Butlerov's term) of an even number of units of affinity. At that time, of course, there could be no discussion of the nature of units of affinity or of the interatomic bond. There was still no clear demarcation between the spatial arrangement and the mutual atomic linkage, and the term "constitution" began to lose its original specificity. The absence of a generalization that could integrate the advances of theoretical chemistry hindered its further development. It was A. M. Butlerov who supplied this generalization in the form of the concept of chemical structure: "Starting from the idea that each chemical atom entering into the composition of a substance takes part in the formation of that substance and acts here with a definite amount of its inherent chemical force (affinity), I call chemical structure the distribution of the action of this force, due to which the chemical atoms, directly or indirectly influencing* one another, become combined into a chemical particle" [1]. Subsequently, Butlerov more laconically defined chemical structure as "the order of chemical bonding existing between atoms in a molecule" [2]. Hence the concept of chemical structure as well as of the order of mutual bonding of atoms in a molecule was the natural result of the whole previous development of science. In the words of Butlerov, "historical necessity led to the theory of chemical structure" [3].

In formulating the concept of chemical structure A. M. Butlerov turned away from the idea of the mechanical structure of molecules. The necessity for this new path was acutely recognized by him. On the one hand, as he wrote, "chemistry, being concerned with matter in a state of transformation, cannot without the help of physical investigations evaluate the mechanical structure of substances" [4], and the possibilities of physical methods of investigation at that period in history were still inadequate for the evaluation of the spatial distribution of atoms, although Butlerov often emphasized that the spatial distribution of atoms would in the future also be amenable to determination; on the other hand, chemists still did not know "of that bond which exists inside the molecule between the mutual chemical action of the atoms which constitute it and their mechanical distribution" [4], while the "chemical properties of the molecule are regarded predominantly as the chemical behavior of the constituent atoms" [4], i.e., its chemical structure. The latter view received spectacular confirmation in the clarification of numerous cases of isomerism: "The principle of chemical structure", said Butlerov, "leads to the a priori assumption of the existence of known isomers" [5]. In the course of time, however, chemists became convinced that the number of actually existing isomers, corresponding to a given empirical formula, exceeds the number of isomers possible on the basis of the theory of chemical structure. The facts compelled them, in the words of Wislicenus [6], "to explain the diversity of isomeric molecules with an identical structural formula by a different arrangement of their atoms in space and to search for definite theories about this arrangement". V. V. Markovnikov voiced the same ideas [7]: "Concerning the grouping of atoms, it (the theory of structure) can in no way wish to touch on the problem of the relative spatial arrangement of atoms.... That is why the former expression "constitution" had to be replaced by the term "chemical structure"... It is difficult, however, to conceive that there do not exist direct and specific relationships between the chemical interaction and physical position of the atoms in the molecule. Finally, there exist certain circumstances, certain facts, which point very strongly to the existence of such relationships. What precisely these are we cannot yet say, but this is one of the most pressing problems which must be solved by some means or other". Two years after these remarks, the first publications of van't Hoff and Le Bel on stereochemistry appeared — the doctrine of the relative position of atoms in space. The perfecting of physical methods of investigation has permitted in our time the determination of the equilibrium interatomic distances and valence angles in absolute units. Chemists are now in a position to study the geometry (or, as A. M. Butlerov said, the mechanical structure), of molecules and have thus scored a fresh success for the theory of chemical structure.

But the solution of the problem of molecular geometry has left many problems still unsolved. Foremost among these are the reactivity of organic compounds, the generalization of the accumulated experimental material, and the discovery of the mechanism of reciprocal influence of atoms in a molecule. Still unclarified is the nature of valence and the chemical bond, on the understanding of which rests the classical theory of chemical structure. The discovery of the electron and of the theory of atomic structure have in large measure led to a solution of these problems. The role of valence electrons in interatomic bonds has been cleared up: quantum mechanics has accounted for the direction of bonds in space and for their saturation and has introduced the ideas of the electron cloud with an irregular electronic "density" of the difference between σ- and π-electrons, of the differing arrangement (and properties) of the σ- and π-electronic density and of the electronic density of the inner shells of the atom. All this signifies another step forward in the understanding of the structure of molecules.

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* We may note that Butlerov often used the word "influence" in the sense of "bond" or "union" of atoms and his term was translated, as in the present case, into German by the words "Zusammenhang" or "Bindung", but strictly the Russian word for "influence" is rendered in German by "Einfluss".

At the present time, consequently, the concept of chemical structure of molecules embraces the ideas of the order of combination of atoms among themselves, of the position of atoms (nuclei) in space, i.e. of the geometry of molecules, and of the distribution of electron density in molecules*.

We are of the opinion that such a concepti .. of the chemical structure is most in harmony with the history and contemporary ideas of the structure of molecules. It is natural that further progress in the field of the structure of matter will enrich the content of the theory and render it more precise.

II

The mechanical types of Dumas showed with particular clarity the attempts of chemists to express the functional dependence of the properties of chemical compounds on the spatial distribution of the atoms. Kekule wrote in 1859 that "the relative position (relative Stellung) of individual atoms has a definite influence on the nature of compounds" and that although it is impossible to present a proved theory of the nature of the relative position, the existence of such an influence was clearly reflected in "the difference of properties of compounds possessing the same composition", i.e., isomers. This very faulty concept of the exclusive dependence of the chemical properties of compounds on the relative position of their atoms divided the great majority of the chemists of his day.

It is therefore impossible to deny the enormous revolutionary significance of the above-enunciated theory of A. M. Butlerov to the effect that "the chemical properties of a molecule are predominantly governed by the chemical interplay** of the component elements" [4]. This idea is expressed still more clearly by Butlerov in the words: "The well-known rule that the nature of a molecule is governed by the nature, number and arrangement of the elementary component parts should now, in my opinion, be changed to the following form: The chemical nature of a molecule is governed by the nature of the elementary component parts, their number and their chemical structure" [9]. Butlerov thus formulated to his contemporaries the following policy ("...we shall concern ourselves only with those problems which can be solved by chemical experiment [9]): The investigation of the chemical structure of substances with the help of chemical reactions." Work along these lines also released organic chemistry from the "awkward" position which it occupied at the beginning of the sixties of last century. A direct consequence of this "law" is the clarification of isomerism: Insofar as the chemical properties ("chemical nature") of substances depend on composition and chemical structure, for a given composition any difference in properties will be the result of differences in chemical structure. This law was the source of the first ideas and of the entire theory of the mutual influence of atoms in molecules: two isomers possess different properties and constitute two different substances "because the chemical relation of the atoms to one another is not the same in both molecules" or in other words "because the individual atoms of one and the same element in both molecules are not equivalent Two, in themselves, identical and equivalent atoms consequently become nonequivalent due to the difference...in the influence of the other atoms present in the same molecule" [10]. Finally it was this very law that invested chemical structural formulas with profound significance: "...when the general laws of the dependence of chemical properties on their chemical structure become known, then such a formula will be the expression of all these properties" [11]. There cannot be any doubt that this Butlerov law is a focal point in the theory of chemical structure as it was propounded in Butlerov's statement of 1861. It binds together all the remaining ideas and concepts of Butlerov's theory and without it the concept of chemical structure itself would have remained suspended in mid-air. In putting forward his "law" he wrote: "I am far from claiming that this law is completely true and that it adequately expresses all the conditions on which the properties of compounds depend... the later development of the opinion here put forward will show to what exent chemical properties depend on chemical structure and to what extent the propounded law is inadequate..." [9]. Actually, in the later study of organic compounds it became clear that the above law is not always valid, and this fact led, as mentioned above, to the development of stereochemistry, the study of the dependence of properties on the mutual arrangement of atoms in space. But the latter doctrine was able to develop by the study not only of chemical properties, such as the order of chemical bonds in molecules, but also of physical properties (e.g. rotation of the plane of polarization). It is due solely to physical investigations that it became possible to characterize quantitatively the direction of bonds in space. With regard to the study of electronic structure, chemical methods differ from physical methods (study of dipole moments, molecular spectra, energies of formation and transformation, etc.) in being able to supply only indirect information. The importance of physical methods of investigation of molecular structure continuously grows. Not a single contemporary hypothesis relating to the electronic structure of molecules could be considered well-founded if it ignored or contradicted the data of physical methods of investigation.

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* Historically the term "chemical structure" was understood to be restricted to the order of combination of atoms with one another (sequence or arrangement of the bonds) in the molecule which Butlerov always clearly differentiated from the spatial arrangement of atoms. This is chemical structure in its original significance. Nor did Butlerov include the composition ("nature and number of elementary components") of the molecule in the concept of chemical structure; it is obvious that even today there is no need to widen the concept in such a way, since when speaking of chemical bonds chemists always understand the linkages between specific atoms.

**In the German text the term "chemischer Zusammenhang" is used.

Consequently, Butlerov's law, while almost entirely retaining its original formulation (the nature of molecules is governed by their composition and chemical structure) acquires ever wider significance since the nature of molecules embraces both their chemical and physical properties, while chemical structure involves the order of addition of atoms, the geometry of molecules and the distribution of the electronic density. Many-sided study of the relation between properties and structure with the objective of discovering the relevant laws must, it appears to us, be the main route to further creative development of the theory of chemical structure in organic chemistry. This route, just as in the time of A. M. Butlerov, is bound to lead to new advances in our understanding of the structure of organic compounds, and will permit practical solution of the important problems of better utilization of already known compounds and the preparation of new compounds with made-to-measure properties.

III

In the volume entitled "A. M. Butlerov. Collected Studies in Organic Chemistry"* appeared our paper on "A. M. Butlerov and the theory of chemical structure". The main purpose we had in mind when writing that paper on the work of Butlerov was to answer the question: "How did the theory of chemical structure arise and develop and what part was played by A. M. Butlerov?" [12]. In this connection we gave a detailed comparison of the publications of A. M. Butlerov with those of his predecessors and contemporaries, and it was clear from this comparison that the priority in the creation of the theory of chemical structure belongs to our great chemist. We strove to help the reader to become familiar with the content of Butlerov's theoretical studies as expounded in the volume. Finally, we wished to fill a gap left by historians of chemistry by giving an account of his battle as a natural materialist and dialecticist against agnostic and mechanistic attacks on the theory of chemical structure. We believe that we were able to publish in the paper new facts and to examine the situation from a new angle in the light of these new facts. We paid least attention to the modern significance and content of the theory of chemical structure. We decided that it would be out of place to expound our standpoint regarding contemporary problems of the theory of chemical structure in our paper accompanying the researches of Butlerov, a series devoted mainly to the origin and to the first Butlerov period of development of the theory of structure. In our paper, therefore, we did not give a detailed analysis of the present-day content of the concept of chemical structure, although we did point out some new facts about the modern concept for comparison with Butlerov's classical definition. Our comments on this score, as well as our whole paper, were severely criticized by G. V. Chelintsev [13]. We leave the readers to judge whether this criticism was justified.

At the start of his paper G. V. Chelintsev quotes our words: "Naturally the theory of chemical structure did not fully retain its original classical form and was subject to further development. Although A. M. Butlerov considered it necessary to limit the concept. . . of the chemical structure and spatial distribution of atoms *while imparting a provisional character to this limitation* (our italics. G. V. Chelintsev replaced these words by a row of dots —Authors' note), it has long lost its significance for the modern theory of structure. When a modern chemist speaks of the structure of a molecule of an organic compound, he uses the word in the literal sense, i.e. he has in mind the spatial...distribution of the atoms which compose it...the specific polarity of its component parts, etc." [14]. Of course it is permissible to add that the modern chemist is not limited by this, as is evident from the two paragraphs following the quotation by G. V. Chelintsev, but it is impossible to deny that stereochemistry was a necessary deepening of the classical theory of chemical structure; it is impossible to say that the modern chemist does not have in mind the spatial arrangement of atoms when speaking about the structure of a molecule, etc. Without considering our remarks on the matter, G. V. Chelintsev there and then rushes to the attack: "Hence (?) the concept of chemical structure of A.M.Butlerov, which according to B.A. Kazansky and G. V. Bykov fundamentally distinguishes the teaching of Butlerov from the views of Kekulé and Kolbe (p. 563) is declared — from the standpoint of modern chemists — to be erroneous". We wish to point out that on p. 563("A.M. Butlerov. Selected Works ") in general nothing is said about the fundamental distinction between the doctrine of Butlerov and the views of Kekulé and Kolbe or that the fundamental difference between them consists mainly not in the problem of the approach to the spatial position of the atoms, although Butlerov was more optimistic about the feasibility of his concept than were the German chemists. On the point that the teaching of Butlerov was both materialistic and dialectic, we would say that the views of Kekulé and Kolbe were characterized by the agnosticism which is erroneous in the light of dialecticism; Kekulé was also tainted by eclecticism. Having assailed us with the help of only one "hence" on the score that we consider Butlerov's theory of chemical structure to be erroneous, G. V. Chelintsev goes on to attribute directly to us the following statement: "At the end of the second of the above citations from the paper by Kazansky and Bykov it is stated that although Butlerov's concept of chemical structure was erroneous, it..." [15], etc. In the paper in question*, however, there is not the least hint to the effect that "Butlerov's concept of chemical structure was erroneous". Or: "B.A. Kazansky and G. V. Bykov refer to the fact that the erroneous (!) concept of chemical structure of A. M. Butlerov..." [15], etc. He then goes on in the following style: "In their paper Kazansky and Bykov regard the theoretical concept of A. M. Butlerov as some collection of opinions devoid of a clear logical connection" [15]. We consider it necessary to explain that this statement completely contradicts the whole content and tenor of our paper and we must protest against the shamelessness with which Chelintsev converts white into black.

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* As the editors of the volume, we take this opportunity of drawing readers' attention to errors that came to light after publication: On p. 104, line 2 from bottom for "ethylene oxide" read "ethylidene oxide"; p. 112, line 10 from bottom, for "proposed" read "proposal"; p. 225, line 14 from top, for "always" read "of all"; p. 533, lines 4-3 from bottom, for "alkali metals and especially silver" read "the majority of metals"; same page, line 3 from bottom, the word "majority" is to be lowered; p. 675, line 3 fromtop, for "155" read "248".

Chelintsev, as well as other like-minded Soviet chemists, frequently attributes to us erroneous, and sometimes even simply nonsensical, statements in order to create a target for his attacks. Here is one example. G. V. Chelintsev writes: "A red thread through the whole career of A. M. Butlerov...is the idea of the decisive significance of a supermechanical law in chemical phenomena. To say, as do Kazansky and Bykov, that this idea possesses a secondary significance in Butlerov's theory of chemical structure is a gross perversion of the teaching of A. M. Butlerov" [15]. Elsewhere [16] G. V. Chelintsev states that we regard this "idea" as simply fallacious. We are bound to point out that nowhere in our paper is there mention of the significance of the idea of a "supermechanical" law in Butlerov's theory; on the contrary, we differ from the author of "the new structural theory" in not considering ourselves entitled to ascribe to A. M. Butlerov any "ideas" that he did not enunciate.

G. V. Chelintsev also attributes to us such statements as: "now Butlerov's concept of chemical structure is equivalent to the concept of arrangement of atoms in space" [17]; it is alleged that we regard molecules as "certain mechanical aggregates of electrons and nuclei" [17], that "in the light of modern science the concept of chemical structure resolves itself into the concept of a mechanical state" [17]; that "modern chemical science treats the mechanical concept of chemical structure only as the spatial location of atoms in molecules", and so on. In short, G. V. Chelintsev attributes to us the statement that the arrangement of atoms in molecules is governed by the mechanical interaction of the atoms, i.e., he attributes to us the view that prevailed in the second half of the past century. Actually, we, like the overwhelming majority of contemporary chemists and physicists, have in mind — when speaking of the arrangement of atoms in space — an atomic interaction of an electromagnetic character.

We have cited examples of the polemic imagination of G. V. Chelintsev not so much to reconstruct for ourselves the "superlogic" of the attacks made on us by Chelintsev (which is obvious to everybody acquainted with our paper on "A. M. Butlerov and the theory of chemical structure"), as with the objective of showing that sophistry in its crudest form, especially the arbitrary interpretation of citations already commented on by A. N. Nesmeyanov [18], is a favorite weapon of the author of "the new structural theory", both in attacks on others and in defense of his theoretical concepts, about which latter we have something to say below.

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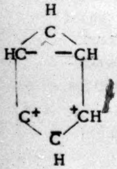
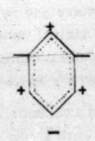
*. We reproduce in full the citation to which Chelintsev alludes and which was artificially made up by him from two disconnected passages taken from different pages: "The concept of chemical structure is nevertheless not basic to Butlerov's theory. The central place in it is occupied by his theory of the dependence of the chemical properties of a compound on its structure" (p.569) . . . However, the Butlerov concept of chemical structure was an essential step forward since,...by drawing a distinction between the concept of arrangement of the bonds of chemical atoms and the concept of the arrangement of physical atoms in space ("the relative arrangement of the atoms"), it expressed the true purpose of the development of organic chemistry — the establishment of the chemical structure of organic compounds" (p558).

As we know, the central concept of Chelintsev's "new structural theory", unanimously rejected by Soviet chemists and physicists (see the transcribed report of the Conference on the Theory of Chemical Structure) is the concept of the homeopolar electrovalent bond. He writes: "The orbit-contact formulas of benzene, ethylene, naphthalene, anthracene, etc. only appear possible in the light of the concept of the homeopolar electrovalent bond" [19], or "In order to be able to write...the formula of benzene, I foresaw (?) the possibility of the homeopolar electrovalent bond" [20]. Actually, without this concept the whole "new structural theory" would not have represented anything original. As far back as 1923, Lowry [21] put forward the suggestion that "whereas a single bond may be either covalent or electrovalent, a double bond in organic chemistry usually reacts as if it consists of one covalent and one electrovalent bond...their existence can be justified on the basis of the electronic theory of valency by assigning a complete octet to each negatively charged atom and a sextet of electrons to each positively charged atom". Lowry represented butadiene by the formula $\overset{+}{C}H_2-\overset{-}{C}H\ \overset{+}{C}H-\overset{-}{C}H_2$, and pointed out that according to his scheme "the distinction between a single and a double bond in conjugated systems disappears completely". Lowry's benzene formula (I), the formulas of butadiene and a series of other compounds differ from the corresponding formulas of Chelintsev [22]: $\overset{+}{C}H_2\overset{\cdots}{-}\overset{-}{C}H\overset{\cdots}{-}\overset{+}{C}H\overset{\cdots}{-}\overset{-}{C}H_2$ and (II), "which express the close multiple bonds of conjugated systems" [23] only by the absence of the dotted line indicating the electrovalent bond. Lowry's formulas have long disappeared from the stage. G. V. Chelintsev tries in vain to infuse new life into them. He writes: "The origin of alternating polarity (in benzene derivatives — authors' note) found its due explanation only in Lowry's formula, but without the concept of contact bonds, this formula could not be proved and therefore it did not receive recognition" [24]. Since Chelintsev himself admits that the "contact bond" is only a "new name" [25] for the electrovalent bond, then the difference between the standpoints of Lowry and Chelintsev resides solely in the fact that, according to Chelintsev, the electrovalent (contact) bond may still be homeopolar.



(I)



(II)

The untenability of the concept of the homeopolar electrovalent bond was repeatedly and convincingly demonstrated at the Conference on the Theory of Chemical Structure. We shall not repeat all the statements, but we find it necessary to expose the sophism of those arguments with which Chelintsev seeks to defend the concept of the homeopolar electrovalent bond. This is all the more necessary since he takes the liberty, in a most unceremonious manner, of attributing to A. M. Butlerov (and not for the first time [26]) his own point of view — which is far removed from Butlerov's point of view.

G. V. Chelintsev "proves" the existence of the homeopolar electrovalent bond by the existence of special "supermechanical relations" between nuclei and electrons, and the well-known (in physics) electric and magnetic interaction between them is designated by a stroke of the pen as a "space-force", mechanical interaction. Of course such a hypothesis of the mechanical character of the electromagnetic interaction between atoms and molecules or between nuclei and electrons is quite untenable (it is, strictly speaking, a mechanical formulation of the problem); likewise there is no justification for the postulation by Chelintsev of certain "supermechanical relations" between nuclei and electrons, this being contradicted by all the existing evidence for physical — according to Chelintsev's definition "mechanical" — relations between them.

We agree with A. N. Nesmeyanov who, in reply to Chelintsev, writes: "A molecule is, of course a nuclear-electronic formation built up in a definite manner, and no special forces enter into its construction, apart from the nuclear-electronic interaction known to physics...the essential feature of a reaction, the essential feature of chemical dynamics consists in the fact that a reaction of one set of chemical substances gives rise to another set of substances, and this essential feature must not be ignored, for it constitutes the specific objective of chemical science. However, this essential feature of a higher (compared with the physical and mechanical) form of movement does not require any special mechanism beyond the known interactions of nuclei and electrons" [27]. The subsidiary purpose of the concept of the "supermechanical" relations between nuclei and electrons—namely, to lend a helping hand to the physically untenable and fundamentally superfluous hypothesis of the homeopolar electrovalent bond—is perfectly obvious. G. V. Chelintsev writes plainly: "The submitted proof[*] of the concept of the homeopolar electrovalent bond is governed by the concept of the supermechanical effect inherent in a system of electrons and nuclei" [28].

However, if we ignore the foregoing "proof", which Chelintsev had to base on the resonance-mesomeric creed, then there are no physical proofs whatsoever of the existence of those very "supermechanical" relations between nuclei and electrons (physicists must still only "concern themselves with this matter", asserts the author of the "new structural theory" [29]). Chelintsev thus takes refuge in historical arguments, attempting to rely on the authority of the Butlerov theory of chemical structure. He placed the sign of equality between his above-quoted concept and the views of Butlerov, from which it follows that the historical advances of Butlerov's theory are a confirmation of the "supermechanical" concept of Chelintsev: "This concept"—the statement continues [28]—"corresponds to the Butlerov concept of chemical structure... Since, as demonstrated by the historical development of organic chemistry, only Butlerov's affirmation of the validity of the formulas of chemical structure leads to an understanding of the laws of chemical phenomena and to their practical exploitation, it is obvious that the concept of the supermechanical relations between electrons and nuclei corresponds to reality". Is it really obvious?

Chelintsev argues that Butlerov put aside "the consideration of the spatial arrangement of atoms", but in addition—and this the author of the "new structural theory" passes over in silence—Butlerov put aside the problem of the nature of the relations of atoms in a molecule, in other words the problem of the nature of the chemical bond, i.e. the very subject on which Chelintsev comments. This is clear from the same passage which Chelintsev himself quotes [30]: "We are fully entitled"—wrote Butlerov—"to speak of the mutual chemical relation of atoms in a molecule as if it were a real relation. *Putting aside the question of the nature of this relation* (our italics - author's note) and the whole of the spatial concepts, we arbitrarily assign to it the name of "link" or "bond". As for the rest, in those rare passages where Butlerov touches on the nature of the interatomic bond, he speaks of interference of movement (e.g. vibration) of one atom by the movement of another atom [32]. In addition, as already noted above, Butlerov put to one side the question of the spatial relations of atoms only temporarily, "in the meantime", a fact that must have been known to Chelintsev. Consequently, the claim of Chelintsev that his concept of the "supermechanical" relations of electrons and nuclei (conflicting with all other ideas about physical interaction) "corresponds to the Butlerov hypothesis of chemical structure" is nothing less than a stain on the reputation of the great Russian chemist—A. M. Butlerov.

Sometimes these dubious "proofs" of G. V. Chelintsev are directly due to that obvious "ignorance of the history of the development of the problem of structure" of which he lightly accuses others and which leads him so far as to deny Butlerov's priority in the creation of the theory of chemical structure. As we know, foreign and some Russian historians have frequently reiterated that structural formulas were already being used by chemists at the end of the fifties of the past century, i.e. chemical structural formulas. This is the chief link in the version first composed by Kekulé and Lothar Meyer, according to which Kekulé was actually the author of the structural theory. Actually, however, even in 1863 (Kekulé was using the type formulas (first edition of the second volume of the textbook of organic chemistry) which, as he himself repeatedly emphasized, are only the formulas of transformation of substances. As V. V. Markovnikov has convincingly shown, even in 1864 Kekulé in his textbook still adhered to formulas of transformation and not of structure: "... the renunciation (of types - Authors' note) is only apparent. No types, but the meaning of the formulas remained as previously" [33]. In contrast to Kekulé's formulas, those of Couper indicated the linkage of atoms in the molecule, but they did not rest on experiment and were governed by the ability of the substances in question to enter into definite reactions. Couper was influenced in their derivation only by the formal rules of valency of elements and, evidently, in the majority of cases he still tended to produce symmetrical formulas. In comparison, therefore, with Butlerov's formulas, those of Couper are arbitrary pseudo-structural schemes.

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[*] It follows, according to Chelintsev, from a comparison of the "new formula of benzene with the hexatriene formula of its pseudomer" that in the transition from the nonexistent "pseudomer" to real benzene an energy gain occurs. In what respect, then, does this "proof" differ from the "proof" of the theory of resonance, according to which a similar energy gain follows from a comparison of real benzene with the resonance form (i.e. the "pseudomer" of benzene), represented by the Kekulé hexatriene formula which Chelintsev has so often anathematized ?

We thus see the profound error of the assertion of the existence of pre-Butlerov structural formulas which more satisfactorily expressed the chemical properties of substances. Furthermore, in the words of Chenlintsev, "structural formulas were written even before Butlerov", but they were regarded as convenient means of expression of the methods of preparation or of the chemical properties" [15] of the molecules. It is clear that these words are only applicable to the type formulas of Gerhardt, Kekulé and their successors. "The instrument which was to be judged the most important instrument in chemical science – writes Chelintsev later – was still very coarsely fashioned but was nevertheless available. However, methods were not known for its utilization. These methods were discovered by A. M. Butlerov" [15]. According to Chelintsev, therefore, Butlerov in his theoretical studies in the early sixties was already utilizing finished structural formulas. The same assertion was made in their time by Kekulé and Lothar Meyer, who did not hesitate to garble historical facts.

Lack of space limited the size of our article and we were unable to deal with other errors of G. V. Chelintsev (knowledge of "mutual influences" on the energy relations of atoms [30], the statement that one of the obstacles to the recognition of his benzene formula has "an ideological character" [28], etc); nor have we composed a final answer to a whole series of his "accusations" and malicious innuendoes, such as : "By the term 'modern chemists' B. A. Kazansky and G. V. Bykov imply only the supporters of the mesomer-resonance theory of Ingold and Pauling" [17].

We have no thought at all of denying the right of G. V. Chelintsev, as well as that of any Soviet scientist, to put forward hypotheses relating to any field of chemistry. We even think that some of our chemists avoid expressing their views on theoretical matters due to fear of criticism, especially when it is so crude and tendentious as that of G. V. Chelintsev, or due to diffidence about the results of discussions, or to disinclination, in general, to enter into polemics. In saying this, we are not reproaching Chelintsev. We willingly acknowledge his services in opposing by positive action the mesomer-resonance theory, the criticism of which by Chelintsev was of undoubted value. Nevertheless, it is impossible to ignore the scientific untenability of the hypothesis of Chelintsev, which he too hastily put forward as a theory. Moreover, its author (forgetting the words of Butlerov: " He who is filled with vain conviction of the truth of his scientific theory is virtually reverting from science to a dogmatic creed" [34] suggests that "other formulas of the chemical structure of conjugated compounds than the formulas of the new structural theory can exist within the framework of modern electron-nuclear concepts" [35]. Consequently, who dares to criticize the new structural theory? How should there be a battle of ideas between other chemists and the author? And any publication opposing his "theory" is made to appear a reprehensible heresy. Anybody writing in opposition to Chelintsev's theory or ignoring it is readily accused by him of "mechanism", "agnosticism", "machism", and similar "isms". Chelintsev prosecutes the campaign for his theory with a vociferous and defamatory slogan: He who is against me is against dialectical materialism. Under the guise of the fight for the dialectic-materialistic development of the Butlerov doctrine of chemical structure, G. V. Chelintsev is at present engaged in defaming existing and potential opponents of his "theory", resorting to methods which cannot fail to shame Soviet chemistry.

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* See Consultants Bureau Translation, pp. 417 ff.

** See Consultants Bureau Translation, pp. 215 ff.

*** See Consultants Bureau Translation, pp. 205 ff.

ELEMENT ANALOGS OF THE PERIODIC SYSTEM

E. P. Ozhigov

In composing his ingenious periodic system, D. I. Mendeleev proceeded from the harmony between the physico-chemical properties of the elements and their masses.

Forced to use only one quantitative characteristic of the element – its atomic weight, D. I. Mendeleev established an interrelationship between the atomic weights and the chemical properties of the elements, and developed the theory for correlation of atomic weights, which was subsequently the object of attention by investigators for 50-60 years of the last century (Dumas, Pettenkofer, L. Meyer, and others).

At the present time these concepts of D. I. Mendeleev have acquired considerable interest in regard to investigation of the periodic properties of the atomic nucleus.

D. I. Mendeleev remarks that "those elements which are similar in chemical properties are either close together in atomic weights (such as Pt, Ir, Os), or increase uniformly and consecutively (such as K, Rb, Cs). Values for the atomic weights of elements belonging to the neighboring long periods differ by approximately 45, for example, K–Rb, Cr–Mo, Br–I. However, elements of a given series possess smaller differences in atomic weights. The differences between the atomic weights of Li, Na and K are the same, approximately 16, for Ca, Mg and Ba the same, for Si–C equal to 16.1, for S–O equal to 16.06 and for Cl–F equal to 16.45. As the atomic weights increase, the elements of one group from two adjacent short periods usually possess large differences (equal to about 20 Ti–Si = V–P = Cr–S = Nb–As, and so forth). For the heaviest elements the greatest magnitudes are reached, for example, 26 = Th–Pb, 26 = Bi–Ta, 25 = Ba–Cd, and so forth, Thus, though not clearly, even with the values of atomic weight for analogs, there is observed a relationship with change in properties [1]."

For the end of the periodic system, D. I. Mendeleev adopts a difference value of 90 between atomic weights of analogous elements (elements of the sixth and seventh periods).

Later, Aston [2] attempted to relate periodic properties of the atomic nuclei with the chemical properties of the corresponding elements. In his monograph he writes: "Examination of a table of mass numbers indicates that there are many instances where a difference of 44 in mass numbers is related to a difference of 18 for atomic numbers. These differences are related to atoms of analogous chemical properties such as Cl^{35}, Br^{79}. Likewise, in a long period a difference of 88 is related to a corresponding difference of 32, for example, Nb^{93}, Ta^{181}". Aston considers these correlations to be purely accidental.

Upon analyzing continuous series of natural isotopes, the authors have come to the conclusion that Mendeleev's values for atomic weight differences of the analogs (applicable to isotopes) reflect nuclear periodicity and represent junction points in the system which relate periodic properties of the atomic nuclei with periodicity in their electronic structures.

The author has established that in the short periods (the second and third) the characteristic difference between the mass numbers for a series of 8, is 16 for a difference of 8 between the atomic numbers, and a difference of 44-48 between mass numbers for a difference of 18 between the atomic numbers of 18 (the medium-length periods), while the characteristic difference in mass numbers is 88-90 for the difference of 32 between the atomic numbers in the long periods. This allows placement of an isotopic series for one period under another period, thus to obtain an isotopic system externally resembling the D. I. Mendeleev's system of elements. The periodicity of elements with even and with odd numbers is shown by an upward displacement for element isotopes with odd numbers, which are quite well reflected in the rules of Shehukarev-Mattay̆kh, Aston and others.

TABLE 1

No.	Periods compared	Differences between periods (in rounded-off units of atomic weight)	
		For the analogous elements, according to Mendeleev	According to the tables for principal isotopes of elements
1	2nd and 3rd	16	16
2	4th and 5th	45	44-48
3	6th and 7th (following the lanthanoids)	90	88-90

For example, from an analysis of a series of isotopes of the second and third periods it can be seen that the pleiads can be arranged under one another in regular fashion, and at the same time those isotopes with similar nuclear structures will possess adjacent values of nuclear spin (Li^7 and Na^{23}, B^{11} and Al^{27}, N^{15} and P^{31}, O^{16} and S^{32}, F^{19} and Cl^{35}). At the same time there also appears a periodic repetition in the chemical properties of the elements; the analog difference of 16 falls within the range indicated by D. I. Mendeleev.

Along with this there are isotopes where the difference of 16 in the atomic numbers is not related to the repetition of chemical properties(B^{10}–Mg^{26}, N^{14}–Si^{30}, Ne^{21}–Cl^{37}); however these exceptions do not violate the general rule, since there cannot exist a perfect mathematical coincidence in difference because of greater increase in number of nuclear neutrons as compared with the number of protons.

It is of interest to mention that the isotopes of greatest life span, among the artificial and the naturally-radioactive elements, correspond to the above-indicated differences. Thus, under isotope Mn^{55} is placed the complete analog – isotope Tc^{99} (a difference of 18 in atomic numbers and a difference of 44 in mass numbers), which possesses a half-life period of $4 \cdot 10^6$ years.

The difference values in atomic weights for the analog elements coincides closely with the difference values for the mass numbers of the principal isotopes of the same elements (Table 1).

TABLE 2

Symbols of elements, and their atomic weights	Th–Ce 232.12-140.13	Pa–Pr 231-140.92	U–Nd 238.07-144.27	Np–Pm 237-147	Pu–Sm 239-150.43	Am–Eu 241-152	Cm–Gd 242-156.9
Difference value. . .	91.99	90.08	93.80	90	88.57	89	85.1

Contemporary science does not give an explanation for this phenomenon, but apparently its basis lies in a periodic construction of the nuclei from specific structural units.

According to modern theoretical concepts [8, 9], protons and neutrons form completed layers in the nuclei, which also determine nuclear periodicity.

A revelation of the role and the significance of D. I. Mendeleev's difference values in atomic weights of element analogs is not only of historical interest, but also possesses considerable significance for elucidation of the problem of methods for development of the periodic system. Inasmuch as the difference value for atomic weights of element analogs fluctuates around a certain average value, and is close to the difference between the mass numbers of their principal isotopes, it might be possible from this average to find the probable mass numbers for the principal isotopes of the new elements which have not as yet been discovered.

As is known, the question of possible new isotopes for elements 96, 97 and 98 is now being debated in the literature.

By making use of the concepts concerning the difference values of atomic weights between elements of the actinide and of the lanthanide groups, this problem might be approximately solved. Atomic weights for the principal isotopes of the transuranium elements have been taken from tables published recently [3].

It can be seen from Table 2 that there exists an abnormally low difference value in atomic weights for the pair, Cm–Gd, indicating that the Cm isotope with mass number 242 is not the principal one.

TABLE 3

Element No. 97

Isotope mass	240	241	242	243	244	245	246	247	248	249	250
Type of radioactive decomposition	K	K	K	K	K	α	α	α	–	–	–
Half-life period	Min.	Min.	Min.	Hours	Hours	Days	Years	Years	Years	Years	Years

Element No. 98

Isotope mass	243	244	245	246	247	248	249	250	251
Type of radioactive decomposition	K	α	K	α	α	α	α	–	–
Half-life period	Min.	Min.	Days	Hours Days	Years	Years	Years	Years	Years

Mass numbers for the principal isotopes of Cm might be determined by systematic addition of the difference 88, and of the difference 90.45 (the average arithmetic value from the element differences preceding Cm) to the atomic weight of Cm.

The resulting numbers 244.90 and 247.35 define not the average atomic weight (average atomic weights for the transuranium elements possess no meaning), but rather the order and the numerical values for the most stable isotopes, including the Cm pleiad. Apparently the mass numbers 243, 244, 245, 246, 247, 248 and 249 should definitely be included in these series. Among the elements of even numbers, more probable is the presence of isotopes of even mass numbers possessing greater half-life periods; therefore, the most stable isotopes should be associated with isotopes of mass numbers 246 and 248. The series presented coincides fundamentally with the series predicted by Seaborg [4].

Similarly, with element 97 the most stable isotopes, with masses 247 and 249, result from adding the differences 88 and 90 to the atomic weight of Tb – 159.2. The principal isotopes for element 98 could be obtained by adding 88 and 90 to the atomic weight of Dy which is equal to 162.48. In such a case, the principal isotopes for element 98 would be 250, 251 and 252. These data for the principal isotopes of the elements Bk and Cf are in satisfactory agreement with the data of A. P. Znoiko [5] and of I. Selinov [6], resulting from other theoretical concepts. We shall present a theoretical series of isotopes for the elements according to A. P. Znoiko [5].

I. Selinov [6] continues the isotopic series for element 98 with mass numbers: 252 |α| 253 |β^-| 254 |α| 255 |β^-| 256 |β^-|

It can be seen from Table 3 that the Mendeleev atomic weight differences for the element analogs have not lost their significance up to the present day.

Taking into account D. I. Mendeleev's observations concerning element pairs (discussed in the works of S. A. Shchukarev [7]), and the fact that difference values in the atomic weights of element analogs of the periodic system coincide with difference values in the mass numbers of isotope analogs, the conclusion might be drawn that to D. I. Mendeleev belongs the priority of having demonstrated, along with the chemical periodicity, a certain nuclear periodicity, the significance of which, in view of the status of science in his time, was not clear to him.

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IONIC RADII AND IONIZATION POTENTIALS

K. B. Yatsimirsky

The ionization potentials are known for a majority of the chemical elements. The existence of a tremendous amount of experimental material in this field has made it possible to work out generalizations and to derive a number of functional relationships between the ionization potential values and characteristics of the atoms. These functions in a majority of cases extend only to atoms with a minimum number of electrons. The validity of periodicity for the ionization potentials with increase in Mendeleev number has been established.

A great number of empirical and semi-empirical equations have been proposed [1] for calculating the ionization potentials of isoelectronic atoms and ions. Some authors, and in particular Wasastjerna [2], have established a relation between the ionization potential values and the distance between nucleus and electron. Undoubtedly there exists a relation between ionization potential and the radius of the ion formed in the ionization process.

An increase in nuclear charge (the Mendeleev number) should lead to an increase in the ionization potential; however, the radius increase formed in the ionization process should lead to the reverse effect. The empirical equation (1) proposed by the author reflects the reverse action of these two factors:

$$I = \frac{A \log Z + B}{r^{3/2}} \qquad (1)$$

In this equation I = Ionization potential, r = radius of the ion formed (the author used Goldschmidt's ionic radii in all cases), Z = Mendeleev's number (atomic number), A and B = constants.

Equation (1) can be slightly modified:

$$Ir^{3/2} = A \log Z + B. \qquad (2)$$

After such modification, the right side of the equation conforms completely to the expression for changes in thermochemical values as proposed by A. F. Kapustinsky [3].

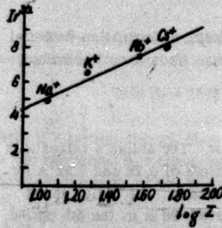

Fig. 1. Graph of the Ionization Potential Dependence Upon Atomic Number.

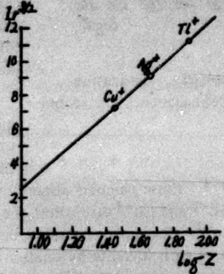

Fig. 2. Graph of Ionization Potential Dependence upon Atomic Number.

In the graphs given (Figs. 1,2,3 and 4) it has been demonstrated that the derivative $Ir^{3/2}$ is actually found to be a linear function of the atomic number. At the same time there appear two groups of ions which appear to differ sharply: a) ions with the inert gas structure (8-electron ions); and b) ions with d- and s-electrons (18-, 18 + 2-electron ions, and also incomplete electronic structures).

The A and B constants in Equation (1) were found with the aid of the graph given. Upon substitution of the numerical values for these constants into Equation (1), the following equations resulted:

$$I_1 = \frac{4.9 \log Z}{r^{3/2}}, \qquad (3a)$$

$$I_1' = \frac{8.8 \log Z - 5.5}{r^{3/2}}, \qquad (3b)$$

$$I_2 = \frac{14.6 \log Z}{r^{3/2}}, \qquad (3c)$$

$$I_2' = \frac{33.3 \log Z - 29.0}{r^{3/2}}. \qquad (3d)$$

Equations (3a) and (3c)define, respectively, the ionization potentials for one and for two electrons in those cases where the basic structure is that of an inert gas. If the basic structure remaining after ionization has a different structure, then Equations (3b) and (3d) should be applied for calculation of the ionization potentials for the 1st and 2nd electrons.

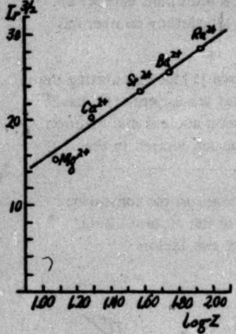

Fig. 3. Graph of Ionization Potential Dependence Upon Atomic Number.

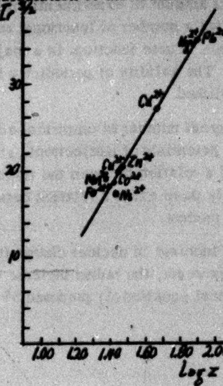

Fig. 4. Graph of Ionization Potential Dependence Upon Atomic Number.

The author has used Equations (3b) and (3d) to calculate ionic radii, since the data for ionization potentials are more extensive than data for ionic radii values. Calculation results are presented in Table 1. Primary data for the ionization potentials were taken from Lisitsin's abstract.

A majority of the ionic radii values given here have been calculated for the first time; however, some of them were reported earlier in the literature.

B. F. Ormont [4] quotes values of 0.76 and 0.72 A, respectively, for the ionic radii values of Ti^{+2} and V^{+2}. These numbers almost coincide with the ones calculated by the author. The author's values with respect to Pd^{+2} and Cu^{+2} differ from the values quoted by B. F. Ormont. He gives values of 0.72 and 0.51 A for Pd^{+2} and Cu^{+2}. The author considers that the last two values differ from the actual values. The radius of the Pd^{+2} ion (0.72 A) is found to be smaller than the radius for the Ni^{+2} (0.78 A). Moreover, Pd is in the 5th period and Ni in the 4th; and, further, the ions for elements of the same group increase with an increase in atomic number. According to experimental data, the similarly-constructed NiF_2 and PdF_2 distances, M and F are respectively equal to 2.00 and 2.15 A, i.e., the radius of the Pd^{+2} ion is larger by 0.15 A than the Ni^{+2} radius, which is in approximate agreement with the author's data.

According to B. F. Ormont [4], the value for the ionic radius of Cu^{+2} differs sharply from the radii of doubly-charged ions for all elements of the 4th period sub-groups. The Cu—F distance in the CuF_2 lattice is 2.34 A [4], which likewise does not agree with Ormont's data.

By utilizing the entropy value for the Cu^{+2} ion in aqueous solution, A. F. Kapustinsky calculated the radius value for this ion [5]. It was found to be equal to 0.82 A; this value coincides well with the one calculated by the author.

The Sn^{+2} ionic radius value (1.17 A) differs somewhat from the value calculated by A. F. Kapustinsky [6]. This difference is explained by the fact that thermochemical calculation of the Sn^{+2} radius was carried out by the use of a first approximation equation for lattice energy (and further, A. F. Kapustinsky obtained a more accurate equation [7]), and in addition, in calculating the radius, the author proceeded from a hypothesis concerning the type of ionic relation in the compounds $SnCl_2$ and SnS. Meanwhile, the type of relation evidently differs from the ionic type, and the A. F. Kapustinsky equation gives somewhat lowered results.

The Ge^{+2} ionic radius value (0.98A) found by Powell and Brewer differs but little from the one calculated by the author.

To verify the ionic radii values obtained, the author, utilizing them, has calculated the lattice energies for tin, chromium, vanadium and indium. The required thermochemical data for compounds of the remaining elements are not available.

TABLE 1

Radii of Certain Ions, Calculated from the Ionization Potentials[*]

Ion	Atomic number	Total ionization potential (electron volts)	Radius (in Angstroms)	Ion	Atomic number	Total ionization potential (elec tron volts)	Radius (in Angstroms)
monovalent ions				divalent ions			
Ni^+	28	7.61	0.96	Cr^{+2}	24	23.3	0.81
Ga^+	31	5.97	1.17	Cu^{+2}	29	27.9	0.80
Pd^+	46	8.3	1.05	Ga^{+2}	31	26.4	0.85
In^+	49	5.76	1.38	Ge^{+2}	32	23.9	0.93
Pt^+	78	8.88	1.16	Pd^{+2}	46	28.1	0.96
divalent ions				Ag^{+2}	47	29.0	0.95
				In^{+2}	49	24.57	1.07
Ti^{+2}	22	20.4	0.77	Sn^{+2}	50	21.9	1.17
V^{+2}	23	~20.8	~0.73				

In the compounds investigated, the type of relation differs from the ionic: therefore, to calculate the lattice energy, the author used an equation developed earlier [9]:

$$U = U_i + 250[0.5 + 0.002(I_2 + 1/4\theta - 2E + D_{x_2} - U_i)]^2, \tag{4}$$

where U = lattice energy; U_i = lattice energy calculated from the Kapustinsky equation; I_2 = ionization potential for two electrons; θ = characteristic temperature for the metal; E = electronic affinity of the x atom, and Dx_2 = dissociation energy of the x_2 molecule.

TABLE 2

Lattice Energies for Certain Salts

Compounds	Lattice energy		Compounds	Lattice energy	
	according to equation (kcal)	from experimental data (kcal)		according to equation (kcal)	from experimental data (kcal)
$SnCl_2$	545	538	$CrCl_2$	617	604
$SnBr_2$	630	637	CrI_2	585	584
SnI_2	516	515	VCl_2	600	589
$Sn(OH)_2$	630	637	$InCl_2$	562	578

The lattice energy value calculated from Equation (4) is given in Table 2. Data necessary for calculations were taken from sources [9] published earlier and from tables compiled by Britske and Kapustinsky [10].

The values calculated according to Equation (4) were compared with those calculated from experimental thermochemical data. There was observed in all cases a satisfactory conformity between calculated and experimental values.

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[*] After dispatch of manuscript to press, the radius of the Francium ion (Fr^{+1}) was calculated by Finkelburg and Stern and was found to be equal to 1.78 Å.

Having now at one's disposal a considerable amount of data for the radii of mono- and of divalent ions, certain regularities can be detected in ionic radii modifications during change in atomic number (Mendeleev number). A compilation of the ionic radii is given in Table 3.

TABLE 3

Radii of Monovalent and Divalent Ions

Atomic number	Ion	Radius	Atomic number	Ion	Radius	Atomic number	Ion	Radius
5	Li^+	0.78	4	Be^{+2}	0.34	32	Ge^{+2}	0.93
11	Na^+	0.98	12	Mg^{+2}	0.78	38	Sr^{+2}	1.27
19	K^+	1.33	20	Ca^{+2}	1.06	46	Pd^{+2}	0.96
28	Ni^+	0.96	22	Ti^{+2}	0.77	47	Ag^{+2}	0.95
29	Cu^+	0.96	23	V^{+2}	0.73	48	Cd^{+2}	1.03
31	Ga^+	1.17	24	Cr^{+2}	0.81	49	In^{+2}	1.07
37	Rb^+	1.49	25	Mn^{+2}	0.91	50	Sn^{+2}	1.17
46	Pd^+	1.05	26	Fe^{+2}	0.83	56	Ba^{+2}	1.43
47	Ag^+	1.13	27	Co^{+2}	0.82	63	Eu^{+2}	1.25
49	In^+	1.38	28	Ni^{+2}	0.78	80	Hg^{+2}	1.12
55	Cs^+	1.65	29	Cu^{+2}	0.80	82	Pb^{+2}	1.32
78	Pt^+	1.16	30	Zn^{+2}	0.83	88	Ra^{+2}	1.52
81	Tl^+	1.49	31	Ga^{+2}	0.85			

As the atomic numbers of the elements change, the radii of identically charged ions change periodically. Upon transition from the basic 8-electron structures to the d-electron structures, contraction always occurs (K^+–Cu^+, Rb^+–Ag^+, Ca^{+2}–Ti^{+2}, Sr^{+2}–Pd^{+2}, etc.). Upon filling in the d-levels, an approximate stability for the ionic radii(Ti^{+2}–Zn^{+2}, Pd^{+2}–Cd^{+2} etc.) is maintained. With respect to this fact, the ionization potential constantly increases with increase in atomic number of the element. When the s-levels are filled in with electrons, a sharp increase in ionic volume is observed (Zn^{+2}–Ge^{+2}, Cd^{+2}–Sn^{+2}, Hg^{+2}–Pb^{+2}, Ag^+–In^+, etc.), and in connection with this a certain decrease of the ionization potential.

For the groups of the periodic system, there is always observed an increase in ionic radius with increase in atomic number. The ionic radii increases slow down somewhat after the lanthanide groups (lanthanidal contraction). Connected with this circumstance are exceptionally high ionization potential values for a majority of the sixth period elements, and a high stability (18 + 2) for the electronic structure of this period (Tl^+, Pb^{+2}, Bi^{+3} etc.).

SUMMARY

1. An empirical equation establishing a relationship between the ionic radii and ionization potentials has been proposed.

2. Ionic radii have been calculated for 15 ions, the accuracy for some of the values of which have been verified by calculation of the lattice energies of the salts.

3. Common mechanisms for changes in the radii of identically-charged ions of the D. I. Mendeleev periodic system have been established.

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A PHYSICO-CHEMICAL INVESTIGATION OF THE SYSTEM $NH_4Br \cdot Al_3Br_9 - C_6H_5NO_2$

(ELECTROCONDUCTIVITY, VISCOSITY AND SPECIFIC GRAVITY)

I. S. Bigich and B. V. Sakhnovskaya

In the preceding works [1] it has been demonstrated upon calculation of viscosity in the region of high concentration, that the molecular electroconductivity for nitrobenzene solutions of aluminum bromide complex compounds assumes an abnormal character. The existing theories of abnormal molecular electroconductivity can be reduced to essentially two opposing theories. The first theory explains the abnormal course of the curves μ and φ on the grounds of disruption of the current-conducting complexes [2], and the second, being based upon the modern concept of liquid body structure, allows that in concentrated solutions there exists a definite order, characterized by the presence of structural groupings which possess internal conductivity. Upon dilution these groups diffuse to form ion pairs, as the result of which a fall in molecular electroconductivity [3] is observed.

According to the latter theory, an abnormal course of the μ-φ curve should appear for all concentrated solutions in calculation of viscosity. The authors considered it necessary to verify this statement by an investigation of the system $NH_4Br \cdot Al_3Br_9 - C_6H_5NO_2$. The composition of such a compound was established by thermal analysis [4].

Electroconductivity, viscosity and specific gravity measurements, and preparation of the $NH_4Br \cdot Al_3Br_9$ complex solutions were carried out in exactly the same manner as was described in the preceding articles [1]. Solutions of the required concentrations were prepared in quantities which permitted simultaneous measurements of electroconductivity, viscosity and specific gravity. Before dissolution, the complex was fused. Dissolution of $NH_4Br \cdot Al_3Br_9$ complex in nitrobenzene proceeded with heat evolution. The color of the solution changed from straw-yellow to red-brown with increase in concentration. During the experiments the vessel for measurement of electroconductivity, the viscosimeter and the pycnometer containing the solution to be investigated were placed in a water thermostat. The temperature in the thermostat fluctuated within the range of ±0.05°.

By investigations on the electroconductivity of the binary system $NH_4Br - AlBr_3$ in benzene [5], xylene [6], ethyl bromide [7] and nitrobenzene [8] it was established that the specific electroconductivities for the solutions increase with increase in concentration of ammonium bromide. Investigators explain the increase in specific electroconductivities for ternary systems as compared with binary systems upon the basis of current-conducting complex formation.

I. S. Bigich [1] investigated the electroconductivity of the $NH_4Br \cdot Al_2Br_6$ complexes in nitrobenzene, in the concentration range 5.01 to 60.25%, and temperature range of 20-50°. The investigation has shown that as the concentration of complex increases, the specific electroconductivity passes through a maximum and then decreases. The maximum for the curve corresponds to 25-30% of the complex. With increase in temperature, the electroconductivity increases, and the curve maximum shifts to the side of higher electrolyte concentration.

Results of measurements on specific electroconductivity, as investigated by the author for the system $NH_4Br \cdot Al_3Br_9$ in nitrobenzene, are graphically presented in Figure 1.

The specific electroconductivity for this system, as with the system $NH_4Br \cdot Al_2Br_6$ in nitrobenzene, passes through a maximum at 25-30% concentration with an increase in concentration of the complex $NH_4Br \cdot Al_3Br_9$. An increase in temperature shifts the maximum toward higher concentration.

The authors have calculated the electroconductivities for the same solutions, corrected for viscosity, and likewise for specific electroconductivities. The calculation was carried out according to the formula $\kappa' = \frac{\kappa \eta_s}{\eta_0}$, where κ = the corrected specific electroconductivity, κ', η_s and η_0 = specific electroconductivity, solution viscosity and nitrobenzene viscosity, respectively.

As can be seen from Figure 2, the maximum on the specific electroconductivity curves disappears when a correction for viscosity is introduced, and the curves themselves possess a convexity toward the abscissa axis.

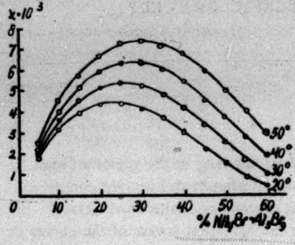

Figure 1. Specific electroconductivity of $NH_4Br \cdot Al_3Br_9$ solutions in nitrobenzene.

The curves of Figure 3 express the relation of molecular electroconductivity to dilution, as calculated for an electrolyte of the composition $NH_4Br-Al_3Br_9$.

As can be seen from Figure 3, the molecular electroconductivity curves also possess a normal character for aqueous solutions; the molecular electroconductivity values increase with increase in temperature. The molecular electroconductivity of the complex $NH_4Br \cdot Al_3Br_9$ in nitrobenzene is somewhat smaller than for the complex $NH_4Br \cdot Al_2Br_6$. With an increase in temperature, the molecular electroconductivity values increase, especially upon extensive dilution. Calculation of molecular electroconductivity, corrected for viscosity, was carried out according to the formula $\mu' = \frac{\mu \eta_s}{\eta_0}$ which is similar to the formula for calculation of corrected specific electroconductivity.

As can be seen from Figure 4, as the concentration of electrolyte increases, the molecular electroconductivity, corrected for viscosity, first decreases, passes through a maximum, and then increases gradually.

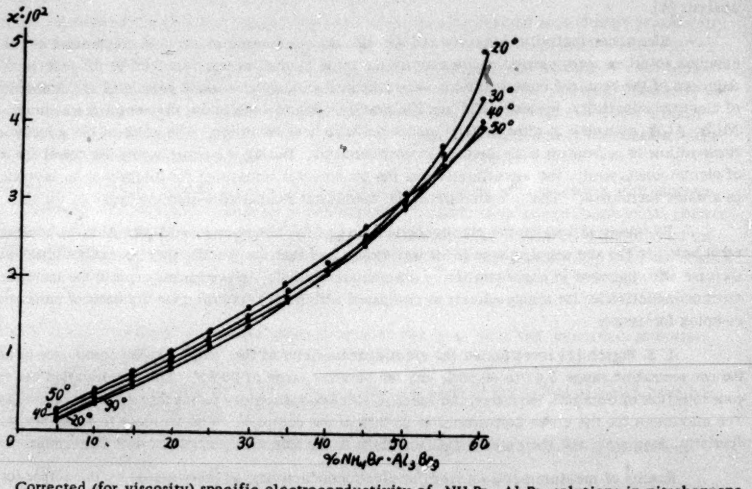

Figure 2. Corrected (for viscosity) specific electroconductivity of $NH_4Br \cdot Al_3Br_9$ solutions in nitrobenzene.

Such a course for the curves of corrected molecular electroconductivity of the solutions investigated indicates that an abnormal course for the $\mu' - (\varphi)$ curves appears in a solution with high dielectric constants upon introduction of a correction for viscosity.

Considering the fact that ammonium bromide does not dissolve in nitrobenzene in the absence of aluminum bromide, and that the dissolution process is related to complex formation, it should be expected, in accordance with the theory of current-conducting complexes, that the complex should be decomposed upon dilution, and that the insoluble component should precipitate out. However, this was not observed. Therefore, the authors consider that their experiments confirm the statement which E. Ya. Gorenbein [3] postulated concerning the nature of the concentrated solutions; any dissolved substance tends to transform into such a state as it might possess in the melted state, and at the same time the highest corrected molecular electroconductivity should correspond to the molecular electroconductivity for the individual electrolyte in the molten state.

In other words, an increase in the molecular electroconductivity, corrected for viscosity, as the electrolyte concentration is increased, depends upon the formation of structural groups which characterize the degree of their regular distribution in the solution. The maximum number of structural associations and also the greatest extent of order corresponds to pure electrolyte in the molten state. As dilution proceeds, there results a disintegration of the structural groups, which results in a decrease of the molecular electroconductivity, as corrected for viscosity. It is characteristic that the temperature effect upon corrected electroconductivity varies in accordance with concentration. In the low concentration range, electroconductivity increases with temperature increase, which is apparently explained by an increase in degree of dissociation, whereas in the high concentration range with temperature increase electroconductivity decreases, which is apparently related to a decreased extent of order for the electrolyte in the solution [3].

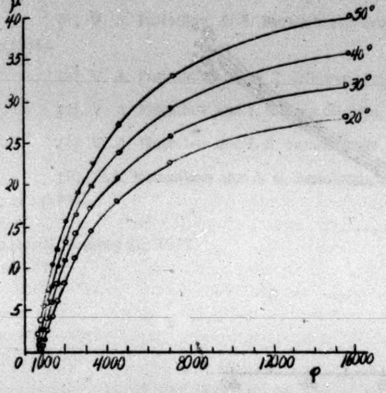

Figure 3. Molecular electroconductivity of $NH_4Br \cdot Al_3Br_9$ solutions in nitrobenzene.

The analogy between the electroconductivity curves of viscosity and of specific gravity for the $NH_4Br \cdot Al_3Br_9$ and $NH_4Br \cdot Al_2Br_6$ complexes which were studied in nitrobenzene gives basis for assuming that the molecular states of these substances in the solution are identical, and that the associations formed are likewise similar. Hence it follows that the mechanism of electric current passage in electrolytes is also identical.

Specific gravity of the $NH_4Br \cdot Al_3Br_9$ complex in nitrobenzene. This was determined under the same conditions as for electroconductivity. The specific gravity was measured by a pycnometer with tightly-ground stopper, on the neck of which were marked divisions to 0.01 ml.

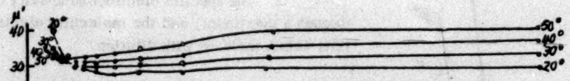

Figure 4. Corrected molecular electroconductivity of $NH_4Br \cdot Al_3Br_9$ solution in nitrobenzene.

As can be seen from Figure 5, the specific gravity for the system increases with an increase in complex concentration. A temperature increase leads to specific gravity decrease, which changes linearly. The d(c) curves possess convexity toward the abscissa axis.

Viscosity. Viscosity measurements for a solution investigated at the same concentration and temperature were carried out in an Ostwald viscosimeter, described in the works of I. A. Katsnelson and A. B. Bernstein [9].

As can be seen from Figure 6, values of solution viscosity for complex concentrations ranging from 5 to 45 % increase slightly at first and the curve slopes, and with further increase in complex concentration the slope of the curve increases sharply.

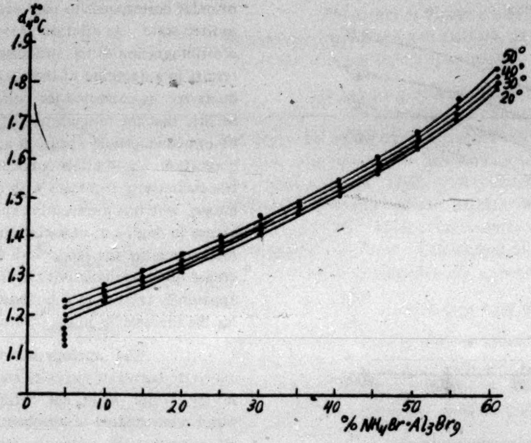

Figure 5. Specific gravity of $NH_4Br \cdot Al_3Br_9$ solutions in nitrobenzene.

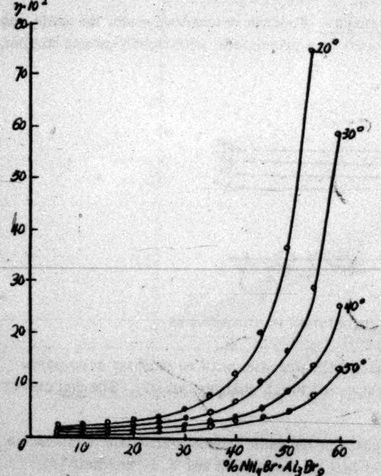

Figure 6. Viscosity of $NH_4Br \cdot Al_3Br_9$ solutions in nitrobenzene.

SUMMARY

1. The electroconductivity, viscosity and specific gravity for $NH_4Br \cdot Al_3Br_9$ complex in nitrobenzene, for the concentration range 5.00 to 60.09%, has been investigated at temperatures of 20, 30, 40 and 50°.

2. The specific electroconductivity curves pass through a maximum, and the molecular electroconductivity values increase with dilution.

3. When corrected for viscosity, the maximum on the specific electroconductivity curves disappears, and the molecular electroconductivity develops an abnormal character. Such a course for the curves confirms the statement postulated by E. Ya. Gorenbein concerning the nature of concentrated solutions.

4. The similarity in the course of the curves for electroconductivity, viscosity and specific gravity for the $NH_4Br \cdot Al_3Br_9$ complexes investigated and for $NH_4 \cdot Al_2Br_6$ [1] in nitrobenzene, indicates that the nature of these systems is probably identical and that the associations formed are similar.

5. The specific and molecular electroconductivities increase with increase in temperature, while the viscosity decreases.

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REFRACTOMETRIC INVESTIGATIONS

I. REFRACTIVE INDEX ISOTHERMS FOR IDEAL SYSTEMS

B. V. Ioffe

The present article is devoted to the problem of the relation of refractive index to the composition of an ideal system. It is usually assumed that for systems which are composed of non-interacting and non-associated components, and which satisfy the thermodynamic conditions for ideality, the refractive index will be found to be a linear function of the composition. However, up to the present time there has been no single viewpoint on which manner of expressing the composition might be considered to give additive refractive indices for ideal systems.

In the first article, which was devoted to refractometry as a method of physico-chemical analysis [1], the additivity of refractive index for ideal systems was utilized as a function of composition expressed in molar units:

$$n_{add} = n_1N_1 + n_2N_2 \qquad (1)$$

(n_1 and n_2 = the refractive indexes and N_1 and N_2 = the molar units of first and second components, respectively).

This position was substantiated by experimental data for the system, bromoform-chloroform, and for mixtures of "isofluid" liquids (isomeric xylenes, esters and others) which were investigated by O. M. Morguleva [2]. Assumption (1) is accepted by most authoritative manuals [3,4], and in a majority of the works on the refractometric physico-chemical method of analysis [5,6,7,8]. However, some authors [9,10,11] consider the refractive index for ideal systems to be a linear function of composition by weight (P) and not by molecular units:

$$n_{add} = n_1P_1 + n_2P_2. \qquad (2)$$

Assumption (2) apparently eliminates (1), but nevertheless the same investigators at times utilize in different articles correlation (1) [6,7,8] and correlation (2) [10,11], without reason for their selection.

Back in 1933 MacFarlane and Wright [12] indicated that, proceeding from the physical nature of the light refraction phenomenon, the refractive index of a mixture should be considered a function of composition in volumetric units (V). Using examples from several systems (hydrocarbons and their halogen derivatives) they demonstrated that the correlation

$$n_{add} = n_1V_1 + n_2V_2 \qquad (3)$$

is better fulfilled than (1) and (2). However, the results of this work in physico-chemical analysis were completely ignored. In 1940, M. Usanovich and A. Stepanyants [13] again indicated that the additive rule for refractive indices should be formulated in accordance with correlation (3), and not by (1), but again these recommendations in subsequent articles on refractometry were not given attention, perhaps due to the inadequacy of the work (the authors quoted data for only two systems selected at random). *

An explanation of refractive index isotherms for ideal systems is of major importance for the refractometric method of physico-chemical analysis. Unusual points and extremes in refractive index isotherms rarely occur, and the interaction of components for binary and ternary systems can be evaluated by the sign and magnitude of deviations from additivity, Δn:

$$\Delta n = n_{exp} - n_{add} \qquad (4)$$

It is quite evident that the value and the sign for Δn depend not only upon the nature of the investigated system, but also upon selection of correlation (1), (2) or (3). for the calculation of $\underline{n}_{add}$.**

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* After the manuscript for the present article had been sent to press, Professor N. A. Trifonov (Kazan) brought to the attention of this author the fact that he and his students had independently come to a conclusion concerning additivity, n_D (V)— see footnote to article in J. Phys. Chem. 21, 503 (1947).

** Δn values, calculated according to (4), will be designated $\Delta n(N)$, $\Delta n(P)$ and $\Delta n(V)$, respectively, according to the different assumptions (1), (2) and (3).

The brief review of literature, as given above, indicates that this problem has not been given due consideration.

The experimental procedure for solving the problem in question consists of an investigation of mixtures of non-interacting and non-associating components A and B which differ considerably not only in refractive indexes, but also in densities (d), molecular weights (M) and molar volumes, i.e., corresponding to the conditions:

$$n_A \gg n_B \text{ or } n_A \ll n_B; \tag{5}$$

$$M_A \gg M_B \text{ or } M_A \ll M_B; \tag{6}$$

$$d_A \gg d_B \text{ or } d_A \ll d_B; \tag{7}$$

$$\frac{M_A}{d_A} \gg \frac{M_B}{d_B} \text{ or } \frac{M_A}{d_A} \ll \frac{M_B}{d_B}. \tag{8}$$

Maintenance of these conditions was found to be essential, since it is not otherwise possible to make a well-defined selection between concentration expressions in molar, weight or volume units (%). In addition to the above-indicated conditions, it should be borne in mind that in order to avoid unfounded conclusions due to random selection of systems, all cases of correlation in numerical values for component properties should be investigated. With the three usual methods of expressing concentration in weight (P), volumetric (V) and molar (N) units, the following six correlations are possible:

$$\text{I. } P_1 > V_1 > N_1 \left(\text{at } M_1 > M_2,\ d_1 > d_2,\ \frac{M_1}{d_1} > \frac{M_2}{d_2}\right);$$

$$\text{II. } P_1 > N_1 > V_1 \left(\text{at } M_1 > M_2,\ d_1 > d_2,\ \frac{M_1}{d_1} < \frac{M_2}{d_2}\right);$$

$$\text{III. } V_1 > P_1 > N_1 \left(\text{at } M_1 > M_2,\ d_1 < d_2\right);$$

$$\text{IV. } N_1 > P_1 > V_1 \left(\text{at } M_1 < M_2,\ d_1 > d_2\right);$$

$$\text{V. } V_1 > N_1 > P_1 \left(\text{at } M_1 < M_2,\ d_1 < d_2,\ \frac{M_1}{d_1} > \frac{M_2}{d_1}\right);$$

$$\text{VI. } N_1 > V_1 > P_1 \left(\text{at } M_1 < M_2,\ d_1 < d_2,\ \frac{M_1}{d_1} < \frac{M_2}{d_2}\right).$$

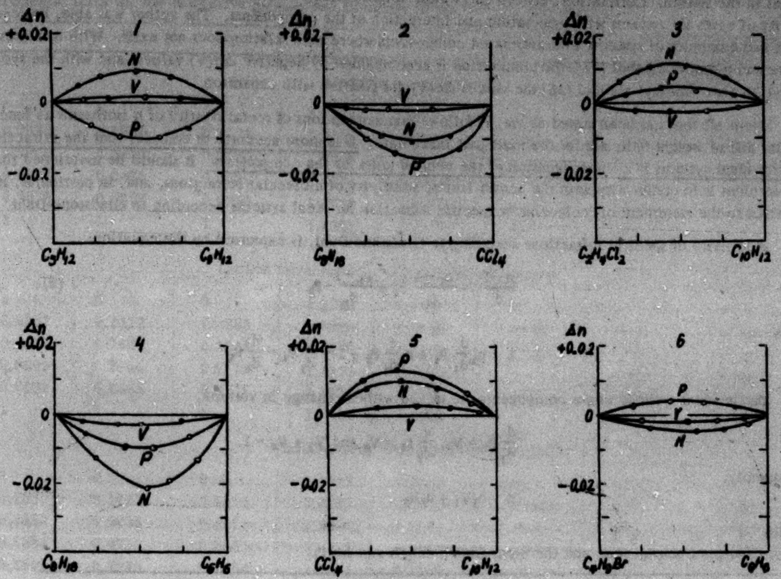
For calculation of Δn in physico-chemical analysis, this method should be used only for expression of compositions where Δn values are determined by the behavior of the components in the mixture, but not by the correlation of their physical properties. For selecting a method of expressing the composition, it is necessary, consequently, to develop the dependence of Δn upon the correlations I-VI. Having available the experimental data for all possible cases [I-VI for conditions (5-8)], a substantiated selection can be made between assumptions (1), (2) and (3).

The author has investigated refractive index isotherms for hydrocarbons and their halogen derivative mixtures which conform to conditions (5-8). The following systems were investigated for all possible combinations of components:

mesitylene — n-pentane (Case I);
carbon tetrachloride — 2,2,4-trimethylpentane (Case II);
bromobenzene — 2,2,4-trimethylpentane (Case II);
tetralin — dichloroethane (Case III);
benzene — 2,2,4-trimethylpentane (Case IV);
tetralin — carbon tetrachloride (Case V);
benzene — n-butyl bromide (Case VI).

The resulting data are presented in Figures 1-7, in the form of curves representing deviations from Δn additivity for various methods of expressing composition. The numbering for systems of the first six figures corresponds to correlations (I-VI), and the component of higher n_D^{20} is considered to be first.

As can be seen from the figures, the smallest deviations in additivity are observed in all cases where concentration is expressed in volume units. The Δn(V) values for the systems examined do not exceed 0.003, while the Δn(P) and Δn(N) deviations reach 0.02-0.03, and at the same time it is quite obvious that the value and sign of Δn(P) and of Δn(N) are definitely dependent upon inequalities I-VI, and consequently are determined not only by their behavior in the mixtures, but also by the correlation of densities and molar volumes for the



Figures 1-6. Deviations in refractive indexes from additivity in relation to various methods for expressing concentration.

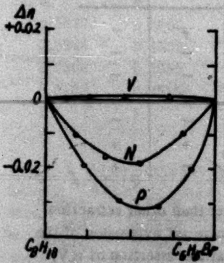


Figure 7. Deviations in refractive indexes from additivity for the bromobenzene-224-trimethylpentane system.

components. The values Δn(P) are positive for the 3, 5 and 6 systems when $d_1 \ll d_2$, and negative at $d_1 \gg d_2$.

In the 1,3 and 5 systems, where $\frac{M_1}{d_1} \gg \frac{M_2}{d_2}$, Δn(N) are positive, and in the 2,4 and 6 systems with $\frac{M_1}{d_1} \ll \frac{M_2}{d_2}$, Δn(N) values are negative. Deviations from additivity, Δn(V), in contrast to Δn(N) and Δn(P) are not connected with correlations I-VI, but are dependent upon system deviations from strict ideality, which show up in volume change upon mixing. The lack of dependence of Δn(V) upon correlations I-VI is illustrated by comparison of all figures given, and is shown with particular clarity in Figure 2 and Figure 7. Data are presented in these two Figures for mixtures of carbon tetrachloride and bromobenzene with 2,2,4-trimethylpentane. Both systems represent Case II of correlations in component properties. In accord with these facts, curves Δn(N) and Δn(P) are very similarly laid out; however, curve Δn(V) in the first system is negative, and in the second, positive.

As can be seen from Table 1, the sign of Δn(V) is determined by the sign of the volume change: if contraction is observed in the system then $\Delta n(V) > 0$; however, if expansion takes place $\Delta n(V) < 0$. The author found no exceptions to this rule for non-interacting and non-associating components, either in his own investigations, or upon searching the literature data.

From Table 1 and from what has been stated above, it follows that, generally speaking, the symbols Δn(N) and Δn(P) are not related to volume change. Attempts to assert this relationship [14] should be considered incorrect.

It should not be thought, however, that deviations from additivity $\Delta n(V)$ are caused exclusively by volume changes in the system. Correlation between $\Delta n(V)$ and volume changes actually take place in an overwhelming majority of cases for systems with association and interaction of the components. The author was able, however, to find two examples of systems with associated components where such relation does not exist. With mixtures of toluene and n-propyl alcohol [14], the contraction is accompanied by negative $\Delta n(V)$ values, and with the system isobutyl alcohol — methyl alcohol [15] the values $\Delta n(V)$ are positive with expansion.

From all that has been stated above, it follows that assumptions of rectalinearity of n isotherms as functions of molar and of weight units are for the most part inaccurate. It is more accurate to consider that the refractive index for ideal systems is a linear function of the volume units for the components. It should be mentioned that this statement is in conformity with the known fact of additivity of molecular refractions, and, in particular, is equivalent to the statement of molecular or specific refraction for ideal systems according to Gladstone-Dahl.

Additivity of specific refraction, according to Gladstone-Dahl, is expressed by the equation:

$$\frac{n-1}{d} = \frac{n_1-1}{d_1} P_1 + \frac{n_2-1}{d_2} P_2. \tag{9}$$

Hence:

$$n = n_1 \frac{d}{d_1} P_1 + n_2 \frac{d}{d_2} P_2 + 1 - \frac{d}{d_1} P_1 - \frac{d}{d_2} P_2$$

But in ideal systems whose components are mixed without change in volume,

$$\frac{d}{d_1} P_1 = V_1, \quad \frac{d}{d_2} P_2 = V_2 \text{ and } V_1 + V_2 = 1.$$

Consequently,

$$n = n_1 V_1 + n_2 V_2 \tag{10}$$

TABLE 1

Volume Changes Upon Mixing, and the Signs $\Delta n(V)$, $\Delta n(N)$ and $\Delta n(P)$

System	Correlation of component properties	Volume change	Signs		
			$\Delta n(V)$	$\Delta n(N)$	$\Delta n(P)$
Mesitylene — n-pentane	I	−	+	+	−
Carbon tetrachloride — 2,2,4-trimethylpentane	II	+	−	−	−
Bromobenzene — 2,2,4-trimethylpentane	II	−	+	−	−
Tetralin — dichloroethane	III	+	−	+	+
Benzene — 2,2,4-trimethylpentane	IV	+	−	−	−
Tetralin — carbon tetrachloride	V	−	+	+	+
Benzene — n-butyl bromide	VI	+	−	−	+

Although it corresponds to experimental data for liquid mixtures somewhat better than other refraction formulas, the empirical formula of Gladstone-Dahl does not appear to be a strict and universal expression of the relation between refractive index and the density of the substance. Hence it follows that the assertion of $n(V)$ additivity for ideal systems in like manner cannot be considered rigorously correct. The form of the isotherms for $n(V)$ systems which satisfy the thermodynamic requirements for ideality can evidently vary somewhat, depending upon the optical properties of the component molecules which determine accurate expression of the refraction formulas for such components.

The problem of importance of refractometric data and, in particular, the $\Delta n(V)$ values, for purposes of physico-chemical analysis, requires further study. In any event, the numerous attempts to relate deviations from additivity $\Delta n(N)$ and $\Delta n(P)$, as being due solely to the interaction or dissociation of components possessing different molecular volumes and densities, should be considered erroneous in the main. Deductions of old works which were based upon such interpretations of $\Delta n(N)$ and $\Delta n(P)$ values, lack sufficient argumentive strength and are in need of revision.

EXPERIMENTAL

For each pair of components 4 mixtures were investigated with concentrations of about 20, 40, 60 and 80%.

TABLE 2

Experimental Data for the Refractive Indexes and Densities of the Systems Investigated

P_1	V_1	N_1	n_D^{20}	d_4^{20}	$\Delta n(P)\cdot 10^4$	$\Delta n(V)\cdot 10^4$	$\Delta n(N)\cdot 10^4$
Mesitylene – n-pentane							
0	0	0	1.3574	0.6259	–	–	–
0.2270	0.1751	0.1478	1.3835	0.6702	–61	+12	+51
0.3960	0.3216	0.2790	1.4045	0.7074	–91	+14	+75
0.6222	0.5435	0.4930	1.4364	0.7618	–94	+18	+90
0.7973	0.7398	0.6990	1.4638	0.8078	–68	+13	+71
1	1	1	1.4994	0.8658	–	–	–
Carbon tetrachloride – 2,2,4-trimethylpentane							
0	0	0	1.3915	0.6918	–	–	–
0.2581	0.1312	0.2053	1.3999	0.8090	–94	–6	–58
0.4252	0.2431	0.3545	1.4073	0.9092	–135	–10	–86
0.5909	0.3854	0.5175	1.4170	1.0368	–153	–11	–102
0.8082	0.6465	0.7578	1.4350	1.2728	–123	–11	–88
1	1	1	1.4605	1.5937	–	–	–
Bromobenzene – 2,2,4-trimethylpentane							
0	0	0	1.3915	0.6918	–	–	–
0.2385	0.1263	0.1856	1.4127	0.7948	–190	±0	–100
0.4383	0.2635	0.3620	1.4364	0.9080	–289	+5	–160
0.6584	0.4710	0.5837	1.4717	1.0750	–307	+9	–180
0.8505	0.7245	0.8054	1.5144	1.2792	–202	+10	–95
1	1	1	1.5598	1.4970	–	–	–
Tetralin – dichloroethane							
0	0	0	1.4448	1.2522	–	–	–
0.1887	0.2306	0.1482	1.4660	1.1848	+27	–14	+66
0.3944	0.4562	0.3277	1.4875	1.1205	+41	–19	+106
0.6066	0.6652	0.5358	1.5081	1.0622	+40	–18	+108
0.8163	0.8513	0.7689	1.5273	1.0101	+26	–8	+73
1	1	1	1.5427	0.9698	–	–	–
Tetralin – carbon tetrachloride							
0	0	0	1.4605	1.5937	–	–	–
0.2045	0.2970	0.2302	1.4872	1.4113	+99	+23	+78
0.3969	0.5196	0.4337	1.5059	1.2726	+128	+27	+98
0.6129	0.7223	0.6482	1.5221	1.1451	+112	+22	+83
0.8270	0.8871	0.8475	1.5343	1.0415	+58	+9	+42
1	1	1	1.5427	0.9698	–	–	–
Benzene – butyl bromide							
0	0	0	1.4397	1.2740	–	–	–
0.1977	0.2632	0.3018	1.4546	1.1686	+28	–13	–36
0.4293	0.5216	0.5689	1.4701	1.0662	+41	–16	–45
0.6198	0.7026	0.7409	1.4812	0.9948	+35	–17	–40
0.8114	0.8619	0.8830	1.4915	0.9324	+20	–11	–24
1	1	1	1.5011	0.8788	–	–	–

The mixtures were prepared in quantities of 20-30 g, and for the 40 and 60% mixtures, weighed portions of pure components (to an accuracy of 1 mg) were taken, while the 20 and 80% mixtures were obtained by dilution of the 40 and 60% by the corresponding components. Re-evaluation of weight units to volume and molar was carried out by the use of special tables $\log \frac{x}{1-x}$ [16].

Preparation of samples of benzene, mesitylene and 2,2,4-trimethylpentane was the same as used by the author in the preceeding works [17, 18]. Technical tetralin was purified from naphthalene impurity by picric acid treatment, followed by vacuum distillation on a column in vacuo (12 theoretical plates). The main fraction with b.p. 93-93.5° at 20 mm was used. n-Pentane (b.p. 35.4-35.9° at 742 mm) was isolated by treatment with sulfuric acid and distillation on a column of a pentane fraction which was kindly supplied by B.A. Bolotov, to whom the author expresses due acknowledgment. Pure market samples of halogen derivatives were dried and distilled in a column.

The refractive index was measured with a refractometer of the Abbe type (Hilger model, year 1948), the scale of which was adjusted in the working range against the readings of a Billingham-Stanley precision refractometer, and was found to be accurate to $1\text{-}2 \cdot 10^{-4}$. Thermostat accuracy was ±0.05°.

Density was determined in Regnault and Byron pycnometers, from 5 to 25 ml in volume.

The benzene-2,2,4-trimethylpentane system was investigated earlier by the author [17]; experimental data for the remaining six systems are given in Table 2.

The author takes occasion to express appreciation to Z. I. Sergeeva for assistance in completion of the work.

SUMMARY

1. The problem of substantiation for the additivity rule of refractive indexes has been investigated, and conditions for solution of this problem by experimental procedure have been indicated.

2. The accepted assumptions of refractive index additivity as a function of the molar and weight proportions, which appear in a majority of the works dealing with the refractometric method of physico-chemical analysis, are inaccurate. The isotherms n–N and n–P for non-interacting, non-associated liquid mixtures may have considerable curvature, depending upon the relation between their molar volumes and densities. The explanation of the n–N and n–P isotherm curvature as being due to the interaction or dissociation of the components is for the most part inaccurate. Deductions in old works, which were founded on an interpretation of $\Delta n(N)$ and $\Delta n(P)$ values, are in need of revision.

3. The statement that in ideal system the refractive index as a function of the volumetric proportions of the constituents is additive is more correct (though not completely rigorous). The small curvature for the n–V isotherms in systems approximating ideality is related to the volume changes which occur upon mixing, but the volume change cannot be considered the only cause of deviation from additivity $\Delta n(V)$.

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NEW REDOX INDICATORS

IV. DIPHENYLAMINO-4-SULFO-2-CARBOXYLIC ACID

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In the preceding works [1,2,3] certain diphenylaminocarboxylic acids were synthesized and tested in the capacity of redox indicators. From derivatives of these acids it was first planned to investigate, in the role of redox indicator, diphenylamino-4-sulfo-2′-carboxylic acid in the form of its sodium and potassium salts, which are described in the literature. The sodium salt was obtained from o-chlorbenzoic and sulfanilic acids [4], and the potassium salt from p-brombenzenesulfonic acid and anthranilic acid [5]. However, upon repeating the first synthesis, it turned out that the substance described is apparently the sodium salt of primary sulfanilic acid. Therefore, a special synthesis of diphenylamino-4-sulfo-2′-carboxylic acid had to be carried out, during which great difficulties were encountered in connection with separation of the free acid. Isolation of the acid was greatly facilitated by its property of producing coloration with dichromate in acid medium, which enabled one to judge the quantity of acid present during various stages of the separation.

Diphenylamino-4-sulfo-2′-carboxylic acid was synthesized by heating the sodium salts of o-chlorbenzoic acid and sulfanilic acids with potash in nitrobenzene or isoamyl alcohol in the presence of copper powder, during which there was simultaneously observed considerable resinification of the reaction mixture. Better results were obtained when the reaction was carried out in aqueous medium in a sealed tube.

Diphenylamino-4-sulfo-2′-carboxylic acid failed to separate as neutral sodium, potassium and barium salts, since the corresponding salts of the initial sulfanilic acid possess the same solubility; diphenylamino-4-sulfo-2′-carboxylic acid precipitated along with sulfanilic acid during precipitation from reaction mixture by hydrochloric or sulfuric acids. Upon further study it was found that the solubility of diphenylaminosulfocarboxylic acid decreased to a minimum at first, with an increase in concentration of hydrochloric acid, but with further increase in hydrochloric acid concentration the solubility of diphenylaminosulfocarboxylic acid increased shartply, and with still higher concentrations again decreased, and sharply.

The first solubility minimum is explained on the basis of "salting out" with hydrogen ion. The subsequent increase in solubility is explained by salt formation, and the final decrease in solubility — by "salting out" with chloride ion. Diphenyl-4-sulfo-2′-carboxylic acid was successfully separated from solutions containing the initial sulfanilic acid in the form of the acid barium salt, which in contrast to the sulfanilic acid barium salt was found to be poorly soluble in water.

The free acid was isolated by decomposition of the acid barium salt with sulfuric acid. For characterization of the diphenylaminosulfocarboxylic acid, its sodium and barium salts were obtained, and also the monomethyl ester. In sulfate medium diphenylamino-4-sulfo-2′-carboxylic acid and its methyl ester form an intense blue-violet coloration in the presence of dichromate and cerium sulfate. The coloration is reversibly decolorized by addition of a reducing agent, and both substances, therefore, can be used as redox indicators.

In conclusion, the author wishes to express sincere appreciation to Prof. A.V. Kirsanov for advice in completion of this work.

EXPERIMENTAL

Diphenylamino-4-sulfo-2′-carboxylic acid. 0.05 mole (11.5 g) of sodium sulfanilate, 0.05 mole (9.5 g) of o-chlorbenzoic acid sodium salt, 0.1 g of copper powder and 0.6 g of copper sulfate were heated in five sealed glass tubes with 20 ml of water for 15 hours at 115-120°. The reaction mixture was filtered and the filtrate acidified with hydrochloric acid to an acid reaction with Congo red. The resulting precipitate was filtered off, dried and, to remove o-chlorbenzoic acid, it was treated several times with small quantities of ether. The precipitate was treated 3 times with 10 ml portions of water, filtrates combined, and saturated barium chloride solution added to the combined filtrates. The resulting acid barium salt was filtered by suction in the form of a fine crystalline precipitate, washed with water, and dried. Yield 5.2 g, or 28.8% of theoretical.

0.2317 g substance: 0.0065 g H_2O. Found %: H_2O 2.80. $Ba(C_{13}H_{10}O_5NS)_2 \cdot H_2O$. Calculated %: H_2O 2.43. 0.2008 g substance: 0.0654 g $BaSO_4$. Found %: Ba 18.58. $Ba(C_{13}H_{10}O_5NS)_2$. Calculated %: Ba 18.51.

To obtain larger quantities, the reaction was carried out in a copper autoclave using 0.5 mole of original acids.

Synthesis of free diphenylamino-4-sulfo-2-carboxylic acid. 5.2 g of the acid barium salt was heated with 10 ml of water and 0.5 ml of concentrated sulfuric acid on a water bath. The hot solution was filtered, brought to 20 ml volume, and 7 ml of hydrochloric acid, spec. grav. 1.19, used to acidify for precipitation of the diphenylaminosulfocarboxylic acid. Solubility of the diphenylaminosulfocarboxylic acid is minimal at a solution acidity corresponding to a hydrochloric acid content of about 20%. The resulting precipitate was filtered off with suction, washed with 20% hydrochloric acid solution and dried over caustic potash, and then sulfuric acid. Repeated purification of the product was carried out by dissolution in water and by precipitation with concentrated hydrochloric acid.

The product failed to crystallize from water because of the very high solubility. The substance dissolves in alcohol upon heating, and crystallizes well, but cannot be filtered off with suction since it is of a consistency resembling gel.

The diphenylaminosulfocarboxylic acid resulting from precipitation with hydrochloric acid is flaky, with a greenish hue, greasy to the touch; difficultly soluble in ether and benzene, decomposes on heating, without melting.

0.3066 g substance: 0.0336 g H_2O. 0.3669 g substance: 22.3 ml 0.1 N KOH. Found %: H_2O 10.83; M 328.8. $C_{13}H_{11}O_5NS \cdot 2H_2O$. Calculated %: H_2O 10.94; M 329.0. 10.18 mg substance: 0.411 ml N_2 (14°, 732 mm). Found %: N 4.62. $C_{13}H_{11}O_5NS$. Calculated %: N 4.77.

Diphenylamino-4-sulfo-2'-carboxylic acid salts. Neutral barium salt. 0.2 g of barium carbonate was added to 2.93 g of the acid dissolved in 15 ml of water. The mixture was heated on a water bath and filtered. After evaporating in vacuo, the residue yielded colorless needles, readily soluble in water, poorly soluble in alcohol.

0.2046 g substance: 0.0164 g H_2O. Found %: H_2O 7.93. $C_{13}H_9O_5NSBa \cdot 2H_2O$. Calculated %: H_2O 7.74. 0.1655 g substance: 0.0898 g $BaSO_4$. Found %: Ba 31.87. $C_{13}H_9O_5NSBa$. Calculated %: Ba 32.08.

Acid sodium salt. 0.53 g of soda ash was added to a solution of 2.93 g of the acid in 5 ml of water. The resulting fine, colorless crystals were filtered off with suction and washed with water. The salt was poorly soluble in water, insoluble in alcohol.

0.4994 g substance: 0.0065 g H_2O. Found %: H_2O 5.60. $C_{13}H_{10}O_5NSNa \cdot H_2O$. Calculated %: H_2O 5.40. 0.2011 g substance: 0.0446 g Na_2SO_4. Found %: Na 7.08. $C_{13}H_{10}O_5NSNa$. Calculated %: Na 7.30.

Neutral sodium salt. 1.06 g of soda in 5 ml of water, as a solution, was added to 2.93 g of the acid dissolved in 10 ml of water. A precipitate of acid salt resulted, which then dissolved completely. The solution was evaporated to dryness in vacuo. After repeated recrystallization from aqueous alcohol, colorless crystals resulted, readily soluble in water, difficultly-soluble in alcohol.

0.2070 g substance: 0.0103 g H_2O. Found %: H_2O 4.97. $C_{13}H_9O_5NSNa_2 \cdot H_2O$. Calculated %: H_2O 5.07. 0.1914 g substance: 0.0788 g Na_2SO_4. Found %: Na 13.66. $C_{13}H_9O_5NSNa_2$. Calculated %: Na 13.32.

Monomethyl ester of diphenylamino-4-sulfo-2'-carboxylic acid. 5.04 g of dimethyl sulfate was added to a solution of 1.46 g of diphenylaminosulfocarboxylic acid in 15 ml of 10% caustic soda, the mixture shaken for 15 minutes, and then acidified with hydrochloric acid. The resulting precipitate was aspirated and washed with water. After recrystallization from aqueous alcohol – colorless crystals resulted, readily soluble in alcohol. The barium salt of the methyl ester was difficultly soluble in water. The melting point was not determined, since the above substance decomposed without melting.

10.43 mg substance: 0.420 ml N_2 (15°, 732 mm). Found %: N 4.51. $C_{14}H_{13}O_5NS$. Calculated %: N 4.56.

To test diphenylamino-4-sulfo-2'-carboxylic acid as a redox indicator, 0.001N solutions of potassium dichromate, cerium sulfate and 0.001M solution of the indicator were used. The total volume of the solutions during testing was 100 ml.

Upon oxidation, the color of diphenylaminosulfocarboxylic acid changed from colorless through yellow-green to a pure blue-violet.

Determination of the acidity range (the lowest normality of sulfuric acid in the solution) at which titration is possible. The dichromate and indicator solutions were added in 4 ml portions to 100 ml of sulfuric acid solutions of varying normality. A suitable color for titration appeared immediately in 10N sulfuric acid solution. At lower solution acidity the color appeared after a certain time. Where ceric sulfate was used, an intense color appeared in 2N sulfuric acid solution; however, this color was less stable: fading rapidly and vanishing.

The smallest quantity of oxidizer and indicator solution possible in 10N sulfuric acid solution at which titration remained possible was 2 ml (optimal quantities 4 ml).

An increase in volume of indicator in the solution above a certain limit did not intensify the color, but imparted a yellowish shade to it. If ferrous ions are present in the solution, then a change in color of the indicator, due to dichromate excess, occurs at lower acidity – in 7.5N sulfuric acid solution.

The possibility for practical application of diphenylaminosulfocarboxylic acid in the capacity of a redox indicator was verified by parallel titration of Mohr's salt solutions along with titration in the presence of known indicators – diphenylaminosulfonic acid and phenylanthranilic acid – at which time deviations in results were observed. Use of large quantities of the indicator should be avoided since it leads to large indicator errors. The latter circumstance does not permit determination of the redox potential for diphenylaminosulfocarboxylic acid.

Properties of the monomethyl ester, as a redox indicator are hardly distinguishable from the properties of diphenylaminosulfocarboxylic acid.

SUMMARY

1. Diphenylamino-4-sulfo-2'-carboxylic acid has been synthesized.

2. It has been demonstrated that diphenylamino-4-sulfo-2'-carboxylic acid may be used in the role of redox indicator when working with strong oxidants.

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* See Consultants Bureau translation, p. 119.

CATALYTIC THERMOPOLYMERIZATION OF ISOBUTYLENE UPON QUARTZ AT LOW PRESSURES

A. D. Stepukhovich and F. M. Mitenkov

During the course of experiments on the thermal decomposition of isobutylene in the region of low pressures and in a temperature range of 811-828°K, in which a spherical quartz flask served as the reactor, the authors encountered an interesting phenomenon. At isobutylene pressures below 2 mm, rather than an increased pressure in the reactor as the result of isobutylene decomposition, a noticeable decrease in pressure was observed instead within the first two minutes, which in some experiments dropped to 20% of the initial pressure. In Table 1 are given data for the influence of initial isobutylene pressure upon the magnitude of relative decrease in pressure within the first two minutes at pressures below 2 mm. As can be seen, the smaller the initial pressure of isobutylene, the greater is the decrease in pressure. The most probable explanation for this fact, in the authors' opinion, is the assumption of isobutylene polymerization which, at these pressures, predominates over the decomposition reaction.

TABLE 1

Pressure Change with Time During the Isobutylene Decomposition Reaction

Test	P_0 (mm)	Per cent pressure change* for same reaction time									
		2 min.	4 min	6 min.	8 min.	10 min.	12 min.	14 min.	16 min.	18 min.	20 min.
						T = 811°K					
15	0.44	- 20.85	- 20.85	- 20.85	- 18.93	- 17.66	–	–	–	–	–
13	0.63	- 18.46	- 18.46	- 18.46	- 17.11	- 16.01	- 15.46	–	- 12.42	–	- 11.58
12	0.85	- 17.14	- 14.79	- 12.41	- 10.04	- 9.99	- 7.55	- 6.55	- 4.31	- 2.55	- 0.51
9	1.29	- 4.13	- 2.09	+ 2.09	+ 5.1	+ 8.49	–	–	–	–	–
17	1.68	- 2.55**	–	–	–	–	–	–	–	–	–
						T = 816° K					
26	0.65	- 16.87	- 14.27	- 14.27	- 8.91	- 7.94	- 5.94	- 2.92	- 2.34	0	+ 2.96
18	1.21	- 8.41	- 6.97	- 4.16	- 2.14	0	+ 2.6	+ 4.35	–	–	–
21	1.86	- 0.86	+ 1.58	+ 3.51	+ 7.09	+ 9.98	+12.55	+14.41	+18.15	+18.54	+20.05
						T = 828° K					
31	0.94	- 5.99	- 3.89	- 0.49	+ 1.23	+ 3.88	+ 6.19	+ 9.98	+12.06	–	–
32	1.08	- 8.06	- 5.65	- 1.37	+ 1.13	+ 3.88	+ 5.78	+ 8.15	+10.54	–	–

The polymerization of isobutylene at pressures below 2 mm of mercury evidently occurs on the walls of the quartz reactor, and appears to be a heterogeneous-catalytic process. The validity of this assumption is indicated by Fig. 1 which shows that the percentage pressure decrease falls to zero, at the same time that the pressure increases to approximately 2 mm,

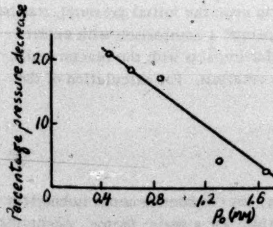

Fig. 1. Relation of Pressure Decrease to Initial Isobutylene Pressure at 811°K.

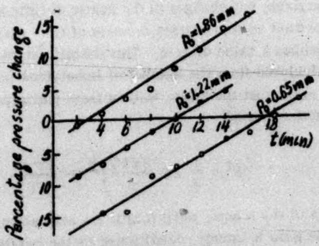

Fig. 2. Relation of Pressure Change to Reaction time for Isobutylene Decomposition (T = 811°K).

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* "-" sign indicates pressure decrease, and "+" sign its increase. ** Further for the 5th, 7th, 9th ... 17th minutes respectively: +0.73, +2.94, +4.81, + 6.68, +8.59, +12.1, +12.43.

and at higher pressures only decomposition takes place, which is accompanied by a pressure increase. As is known, normal polymerization is a homogeneous and bimolecular reaction, and with pressure increase should increasingly prevail over decomposition, due to the fact that pressure would continue to decrease with further increase in primary pressure.

Meanwhile, in the authors' experiments, polymerization is in no way manifested at pressures above 2 mm. Moreover, if it is assumed that under the authors' experimental conditions a normal polymerization takes place, then it appears impossible to explain the initial pressure change in that period of time when the pressure is below 2 mm. The data given in Table 1 indicate that the pressure decrease occurs only within the first two minutes of the reaction, but after that the pressure increases almost linearly with time, as is shown in Figs. 2 and 3. Thus the process which conditions the pressure decrease occurs and is completed within the first two minutes of reaction. After that only isobutylene decomposition proceeds, the rate of which conforms to a first order reaction equation.

The facts which have been discussed lead to the conclusion that at pressures below 2 mm, in the temperature range 811-828° K, catalytic polymerization of isobutylene occurs on the walls of the quartz reactor. We shall now attempt to present a hypothetical picture of this phenomenon. It might be assumed that because of adsorption, the surfaces of the walls are covered with a layer of isobutylene molecules, in all probability of monomolecular layer thickness, upon introducing the gas into the evacuated reactor. Upon impacts of isobutylene molecules with those sections of the walls which are covered with isobutylene molecules, promotion of molecular polymerization may occur due to heterogeneous catalysis.

During the first moments of time this process proceeds so rapidly that the pressure decrease caused by it considerably exceeds the pressure increase which is simultaneously conditioned by the occurrence of isobutylene molecular decomposition. The catalytic polymerization phenomenon, under the experimental conditions defined by the authors, may perhaps take place at any initial pressure. However, at pressures above 2 mm, this process is completed so rapidly that the pressure decrease does not become evident in the experiments. At lower initial pressures the catalytic polymerization rate is smaller, and for its completion requires correspondingly longer time. As a first approximation, this time is inversely proportional to the initial pressure. As the active parts of the surface (or the whole surface) of the reactor become covered with a layer of forming isobutylene polymers, catalysis of polymerization ceases, decomposition begins to predominate, and consequently the increase in pressure within the reactor will begin.

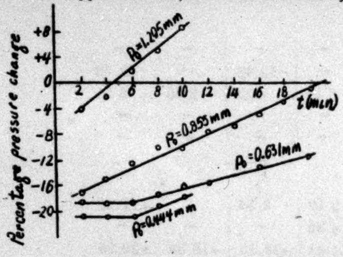

Figure 3. Relation of Pressure Change to Time During Isobutylene Decomposition (T = 816°K).

Actually, after lapse of the first two to four minutes, within which time the pressure decrease takes place, a gradual increase in pressure was observed which was proportional to the reaction time. In addition, having made certain assumptions, it can be demonstrated that the proposed explanation is in quantitative agreement with the experimental data. Let it be assumed that the rate of catalytic polymerization on the wall is defined by the equation

$$W = K^I X, \tag{1}$$

in which X = volume concentration of isobutylene and K^I = the polymerization rate constant, which does not depend upon the concentration of isobutylene, but changes in the course of time up to zero (or to a very small value). It will be considered that K^I is constant up to a certain moment of time (depending upon the initial pressure), starting from which the constant K^I assumes a value of zero. This simplification will permit a comparison with experiment. The K^I value can be calculated from the number of isobutylene molecular impacts with the reactor walls, if the simplified assumption is made that the entire wall surfaces participate in catalysis. For calculation of the K^I value, the following expression was used:

$$K^I = \frac{1}{4}\, aS \left(\frac{2\pi kT}{m}\right)^{\frac{1}{2}} e^{-\frac{E-\epsilon}{kT}} \tag{2}$$

in which S = square surface area of the reactor walls (cm²); E = activation energy for the homogeneous isobutylene polymerization reaction; ε = the gain in energy, conditioned by the catalyst action; a = a steric factor. According to the calculations for isobutylene polymerization [1]: E = 42 kcal./mole, and a = $7 \cdot 10^{-2}$.

Using the radius value for the spherical reactor (r = 4 cm), and assuming that E = 10 kcal./mole, a K^I = value of 0.00043 was obtained at 811°K.

If K_1 = the monomolecular isobutylene decomposition constant, then the concentration change resulting from the two competing processes per unit of time is equal to $\Delta X = (K^I - K_1)X_1$, and for a time interval of Δt respectively $\Delta X \cdot \Delta t = (K^I - K_1)X\Delta t$. Here an assumption will be made concerning the constancy of K^I up to a certain moment in time. The percentage pressure decrease for Δt time can be calculated, which is equal to

$$\frac{\Delta p}{p} \cdot 100 = \frac{\Delta X \cdot KT}{p} \quad \Delta t \cdot 100 = \frac{(K^I - K_1)\, X\Delta tKT}{p} \cdot 100. \qquad (3)$$

Apparently if the pressure change becomes negative by the use of (3), then this indicates that at this moment in time an increase in pressure will result, instead of a pressure decrease, and that decomposition will predominate over polymerization.

TABLE 2

T°K	p_0(mm)	reaction time (in min.)	pressure decrease (%)	
			calculated	experimental
811	1.68	2	3.18	2.55
811	1.29	2	4.36	4.13
811	0.63	6	14.30	18.46
811	0.44	6	14.66	20.85
828	1.08	2	6.93	8.10
828	0.94	2	6.80	6.00

A comparison is given in Table 2 of the calculated and of the experimental pressure drops at an initial pressure below 2 mm of mercury. At the moment in time, t, starting from which, according to the assumption made, K^I can be considered equal to zero, the authors selected this moment of time, experimentally, as that moment at which the pressure decrease is replaced by an increase. Using K_1, calculated values for constants at corresponding isobutylene pressures were taken as (811° K and $p_0 = 1.68$): $K_{1calc.} = 8.76 \cdot 10^{-5}$; $p_0 = 1.29$; $K_{1calc.} = 6.87 \cdot 10^{-5}$ and so forth, (828°K and $p_0 = 1.08$): $K_1 = 0.87 \cdot 10^{-4}$; $p_0 = 0.94$, $K_1 = 0.77 \cdot 10^{-4}$.

SUMMARY

1. In the pressure region below 2 mm, at a temperature between 811-828°K, a catalytic thermopolymerization of isobutylene occurs on the quartz walls, which predominates over decomposition in this range.

2. A hypothetical mechanism for catalytic thermopolymerization of isobutylene for pressures below 2 mm has been given, which agrees satisfactorily with the facts.

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SULFOCHLORINATION

I. THERMAL DECOMPOSITION OF ALKANESULFONIC ACID CHLORANHYDRIDES AS A METHOD FOR DETERMINATION OF POSITION OF THE SULFO GROUP

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Within the past few years the method of introducing the sulfonic acid group into paraffins and cycloparaffins by the action of sulfur dioxide and chlorine with exposure to short wave-length light has gained wide application both in the laboratory and in industrial practice. During this reaction a mixture of the chloranhydrides of the mono- and disulfonic acids results, which is why it is frequently called a sulfochlorination reaction [1].

Determination of the place of entry of the sulfo group offers considerable difficulty since the aliphatic sulfonic acds have received but little study up to the present time; moreover, the sulfochlorides themselves are quite unstable, and distill without decomposition only in vacuo (n-octanesulfonylchloride, and larger molecules distill with decomposition even in vacuo). It is known that [1] upon distillation without vacuum a sulfonyl chloride decomposes readily to form sulfur dioxide and hydrogen chloride and also to form chlorides and olefins. However, up to the present time no systematic study of this reaction has been carried out.

The authors' experiments cited below, for decomposition of several mono- and dichloranhydrides, have shown that in all cases chlorine enters only that position which is occupied by the sulfo group in the initial compound.

The following sulfochlorides were investigated:

1) $CH_3CH_2CH_2CH_2SO_2Cl$ — chloranhydride of butanesulfonic-1-acid;
2) $(CH_3)_2CHSO_2Cl$ — chloranhydride of propanesulfonic-2-acid;
3) $(CH_3)_2CHCH_2SO_2Cl$ — chloranhydride of 2-methylpropanesulfonic acid;
4) $C_6H_5CH_2CH_2SO_2Cl$ — chloranhydride of ethylbenzosulfonic-1^2-acid;
5) $CH_2(SO_2Cl)CH_2CH_2CH_2SO_2Cl$ — dichloranhydride of butanedisulfonic-1,4-acid;
6) $CH_2(SO_2Cl)CH_2CH(SO_2Cl)CH_3$ — dichloranhydride of butanedisulfonic-1,3-acid.

The monochloranhydrides were synthesized from the corresponding chlorides by conversion to the rhodanides, with subsequent treatment of the latter by chlorine. The chloranhydrides were characterized by the melting points of their amides. The dichloranhydrides were synthesized by sulfochlorination of the chloranhydrides of butane-sulfonic-1-acid with exposure to a mercury lamp. From the resulting mixture two isomers were isolated, and their melting points determined. It should be mentioned that according to the literature data [2], the fatty chloranhydrides give very low yields of amides (25-30%) upon treatment with gaseous ammonia. For this purpose the authors recommend amidation by the use of liquid ammonia [3]. By this method, in the authors' experiments, high amide yields (up to 90%) invariably resulted.

Decomposition of sulfochlorides begins above 100°; however, the rate is negligible up to 150-180°. The authors carried the reaction out in an oil bath of 200-220° temperature. Reaction was complete within 1.5-2 hours. The reaction flask was equipped with a reflux condenser filled with hot water of such temperature that the highly volatile chloride formed could be distilled. In this manner the chloride yields were considerably increased (up to 75-85%). For the dichloranhydrides, the reflux condenser was replaced by a fractionating column. The chlorides isolated from the reaction boiled within narrow ranges. They were identified by their boiling points and specific gravities.

In addition, each of the resulting chlorides was then converted into the rhodanide, the chloranhydride, and the corresponding sulfonamide. The latter, by mixed melting point tests, were identified as the chloranhydrides obtained by decomposition. It was thus proved with certainty that an exchange of the SO_2Cl group for the chlorine atom occurs at the same position on the carbon chain without isomerization.

The transformation reaction studied by the authors may be of considerable aid in determining the structure of fatty sulfonic acids. The latter have been but little studied up to the present time; however, the chlorides are known for a great number of various representatives, with well-defined constants, and can be further characterized by conversion into compounds of other classes.

EXPERIMENTAL

Synthesis of Sulfonylchlorides

The Chloranhydride of Propanesulfonic-2-acid. 230 g (2.34 moles) of potassium rhodanide was added to 150 g (1.9 moles) of 2-chlorpropane (d_4^{20} 0.8588; b.p. 36-37°) which was dissolved in 500 ml of ethyl alcohol. The mixture boiled with reflux for 40 hours on a water bath. The reaction mixture was diluted with water. The rhodanide was extracted with ether. The ether extract was washed with water and dried with calcium chloride. After removal of ether, the 2-rhodanepropane was distilled; b.p. 148-150° (745 mm). 160 g resulted (yield 83.3%; d_4^{20} 0.9784.

155 g of 2-rhodanepropane and 1.5 liters of water were introduced into a three-necked, three-liter flask, equipped with stirrer, bubbler for chlorine, and a thermometer. With a continuously operating stirrer, chlorine was let in at such a rate that the reaction mixture temperature did not exceed 20°. Reaction continued until the reaction mass turned yellow from chlorine excess. After completion of reaction, chlorine was removed by a stream of nitrogen. The resulting chloranhydride (a heavy oil of sharp odor) was extracted with ether, and dried with calcium chloride. The chloranhydride was redistilled in vacuo (yield 83.2%). B.p. 71-73° (13 mm). (According to DUge [4], b.p. 79° at 18 mm; d_4^{20} 1.1645.

Found %: Cl 24.81, 24.89. $C_{13}H_7O_2ClS$. Calculated %: Cl 24.91.

The Amide of Propanesulfonic-2-acid. This was obtained in the following manner: 10.2 g (0.072 mole) of the chloranhydride was dissolved in 50 ml of ether, cooled to −40° with alcohol-dry ice mixture, and then added gradually to liquid ammonia (11 g) which was cooled to the same temperature, and placed in a Dewar flask. The mixture was left for 8-10 hours at normal temperature, and was then heated on a water bath to remove ammonia. The solution was separated from ammonium chloride by filtration and diluted with petroleum ether. The resulting amide was recrystallized from ether and petroleum ether mixture. 8.02 g resulted (yield 91.2%). White flakes, m.p. 66° (according to Düge [4], m.p. 60°).

Found %: S 25.97, 25.93. $C_3H_9O_2NS$. Calculated %: S 26.01.

The Chloranhydride of Butanesulfonic-1-acid. 377 g (3.88 moles) of potassium rhodanide was added to a solution of 300 g (3.24 moles) of 1-chlorbutane in 1200 ml of ethyl alcohol. The mixture was boiled on reflux for 60 hours. Processing of the mixture was carried out as above. 281.9 g (75.8) of 1-rhodanebutane resulted. B.p. 182-183°.

Conversion of the rhodanide into chloranhydride was carried out as described for 2-rhodanepropane above. 330.6 g (90% of theoretical) of the chloranhydride of butanesulfonic-1-acid resulted from 270 g of rhodanebutane. B.p. 75-76° (7 mm); d_4^{20} 1.2078. (According to Düge [4], b.p. 96-97° at 18 mm).

Found %: Cl 22.63, 22.67. $C_4H_9O_2ClS$. Calculated %: Cl 22.68.

The Amide of Butanesulfonic-1-acid. This was prepared, as described above for the amide of propanesulfonic-2-acid, from 8.5 g of the chloranhydride of butanesulfonic-1-acid. There was obtained 6.13 g (82.4% of theoretical) of the amide. After recrystallization from a mixture of ethyl and petroleum ethers – white flakes with m.p. 44-44.5° (according to Düge [4], m.p. = 45°).

Found %: 23.32,23.29. $C_4H_{11}O_2NS$. Calculated %: S 23.35.

The Chloranhydride of 2-Methylpropanesulfonic-1-acid. 133.4 g of potassium rhodanide was added to a solution of 200 g (146 moles) of isobutyl bromide in 600 ml of ethyl alcohol. The mixture was boiled with a reflux for 16 hours on a water bath. The reaction mass was processed as before. 123.2 g of 1-rhodane-2-methylpropane resulted (73.2% yield. B.p. 57-58.5°, 8 mm).

The chloranhydride of 2-methylpropanesulfonic-1-acid was obtained from the rhodanide by the action of chlorine, as indicated above. From 115.0 g of rhodanide, 132.0 g (84.0% of theoretical) sulfonyl chloride resulted. B.p. 77-78° (11 mm); d_4^{20} 1.2014 (according to Düge [4], 79.5-80° at 13 mm).

Found %: Cl 22.52, 22.57. $C_4H_9O_2ClS$. Calculated %: Cl 22.68.

Since the amide of 2-methylpropanesulfonic-1-acid is a liquid at normal conditions (according to Düge [4], b.p. = 14-16°), for identification, therefore, the authors used the crystalline cyclohexylamide. 3.0 g of sulfonyl chloride was dissolved in 20 ml of ether, and 8.2 g of cyclohexylamide was added to the solution. The mixture was boiled for 6 hours on a water bath with a reflux condenser. The precipitated hydrochloride of cyclohexylamine was filtered off. After washing with dilute hydrochloric acid, the residue after evaporation of the ether was recrystallized from methyl alcohol. 2.81 g of white needle crystals resulted, with m.p. 56-57°.

Found%: S 14.31, 14.39. $C_{10}H_{11}O_2NS$. Calculated %: S 14.66.

The Chloranhydride of Ethylbenzenesulfonic-1^2-acid. 26.10 g (0.27 mole) of potassium rhodanide was added to a solution of 25 g (0.18 mole) of 1^2-chlorethyl benzene in 150 ml of ethyl alcohol. The mixture was boiled on a water bath under reflux for 40 hours. Processing of the reaction mixture was carried out as before.

19.26 g (66.4% of theoretical) of the 1^2-rhodaneethylbenzene resulted. B.p. 116-118° (3 mm); d_4^{20} 1.2158.

Found %: S 19.58, 19.54. C_9H_9NS. Calculated %: S 19.63.

Conversion of the rhodanide into the sulfonylchloride was carried out with the chlorine treatment as described above. The viscous liquid resulting from the reaction was extracted with ether. The extraction was washed with water and dried with calcium chloride. After evaporation of the ether, the residue partially crystallized on standing. The pressed-out crystals were recrystallized from benzene and petroleum ether mixture. From 16.34 g of rhodaneethylbenzene, 10.45 g (51.10%) of long, colorless flakes, with m.p. 81-82°, resulted.

Found %: Cl 17.29, 17.32; S 15.52, 15.56 . $C_8H_9O_2ClS$. Calculated %: Cl 17.35; S 15.64.

The amide was obtained as above. From 1.2 g of sulfonyl chloride 0.72 g (66.3%) of the amide resulted. After recrystallization from hot water – white, fine needle crystals with m.p. 129-129.5°.

Found %: S 17.24, 17.18. $C_8H_{11}O_2NS$. Calculated %: S 17.29.

The Dichloranhydrides of Butanedisulfonic-1,4-and Butanedisulfonic-1,3-acids. 126.0 g of the chloranhydride of butanesulfonic-1-acid was placed in a three-necked flask equipped with stirrer, bubbler and thermometer, and was treated for 10 hours with a mixture of gaseous chlorine and sulfur dioxide, with exposure to a mercury lamp SVD Sh-250. Chlorine was introduced at the rate of 0.8 ml/sec., the sulfur dioxide – 1.3 ml/sec. At first the reaction mass became green-colored, but decolorized after 20 minutes and remained so to the end of the reaction. The temperature rose from 20 to 40° and was maintained unchanged up to the end of the gas introduction. After 10 hours introduction of gas was complete, and the excess gases were removed by a stream of nitrogen. 173.0 g of colorless oil resulted. The reaction product was fractionally distilled in vacuo. 119.4 g distilled at 60-80° (8mm). The residue in the flask amounted to 50.3 g. The residue, which solidified to a brown crystalline mass, was dissolved in 100 ml of benzene, and was boiled with activated charcoal under reflux to decolorize. During precipitation of the filtrate with carbon tetrachloride, crystals resulted which were then recrystallized from benzene and petroleum ether mixture. 41.2 g of white needles with m.p. 82.5-83° resulted. From its melting point, the resulting substance corresponded to the dichloranhydride of butanedisulfonic-1,4-acid (according to Asinger [7], m.p. = 83.5°.)

Found %: Cl 27.76, 27.71. $C_4H_8O_4Cl_2S_2$. Calculated %: Cl 27.84.

200 ml of petroleum ether was added to the filtrate from the preceding operation. The precipitated crystals were filtered off and recrystallized from benzene and petroleum ether. 6.3 g of white needles with m.p. 40-41° resulted. From its melting point, the substance corresponded to the dichloranhydride of butanedisulfonic-1,3-acid (according to Asinger [7], m.p. = 41°.)

Found %: Cl 27.68, 27.71. $C_4H_8O_4Cl_2S$. Cl 27.84.

Thermal Decomposition of the Chloranhydrides of Sulfonic Acids.

The authors used the following apparatus for decomposition of the monosulfonyl chlorides. The reaction flask was connected by a ground connection to a vertial condenser filled with hot water in such a manner that the chloride vapors forming during the reaction passed on through the condenser. The gases and vapors formed entered into a descending condenser. The condensate was collected in a receiver and trap placed in a Dewar flask filled with water and ice. In experiments with the dichloranhydrides and chloranhydrides of ethylbenzenesulfonic acid, the vertical condenser was replaced by a fractionating column 20 cm in length wrapped with two layers of asbestos.

The Chloranhydride of Propanesulfonic-2-acid. 20 ml (25.28 g) of the chloranhydride of propanesulfonic-2-acid was charged into the reaction flask. The decomposition was carried out at an oil bath temperature of 200-220°. Reaction was complete after 1.5 hours. The combined condensate from receiver and trap was subsequently washed with 3% soda solution and water. After drying with calcium chloride, 10.5 g of the chloride resulted (yield 73.4% of theoretical). B.p. 36-37°; d_4^{20} 0.8565 (according to Leca [5], the b.p. = 36.25° at 760 mm).

Found %: Cl 45.16, 45.15. C_3H_7Cl. Calculated %: Cl 45.22.

For confirmation of the structure of the obtained chloride, it was subsequently converted into the rhodanide, the sulfonyl chloride, and the sulfonamide. The latter was found to be identical with the amide of propanesulfonic-2-acid: m.p. 65-66°, and with no melting point depression for the mixture.

The Chloranhydride of Butanesulfonic-1-acid. Decomposition of the chloranhydride and treatment of the obtained chloride were carried out similarly to that described above for the chloranhydride of propanesulfonic-2-acid. 12.43 g of the chloride (yield 87.9% of theoretical) was obtained from 20 ml (24.16 g) of the chloranhydride of butanesulfonic-1-acid. B.p. was 77-78°; d_4^{20} 0.8892 (according to Leca [5], b.p. = 78.05° at 760 mm).

Found %: Cl 38.28. 38.29. C_4H_9Cl. Calculated %: Cl 38.37.

For confirmation of the structure, the chloride obtained was converted to the amide of butanesulfonic acid with m.p. 44-45°.

A sample of the obtained amide when mixed with the amide from initial chloranhydride of butanesulfonic acid did not show depression in the melting point.

Chloranhydrideof 2-methylpropanesulfonic-1-acid.Decomposition of the sulfonyl chloride and treatment of the obtained chloride was carried out in a manner similar to the preceding cases. 5.95 g of chloride resulted (yield 79.63% of theoretical) from 12.7 g of the chloranhydride of 2-methylpropanesulfonic-1-acid. B.p. was 68-69°, d_4^{20} 0.8800 (according to Linnemann, b.p. = 68.5°).

Found %: Cl 38.34, 38.25. C_4H_7Cl. Calculated %: Cl 38.37.

For confirmation of the structure of the obtained chloride, it was converted into the sulfonyl chloride and then into the cyclohexylamide. After recrystallization from methyl alcohol, it was in the form of fine needles, m.p. 56-57°. Melting test for the mixture also confirmed the identity with cyclohexylamide of 2-methylpropanesulfonic acid.

Dichloranhydride of butanedisulfonic-1,4-acid. Decomposition was carried out at an oil bath temperature of 200-221°. The chloride formed was subsequently washed with sulfuric acid (d. 1.84) and water. From 5.02 g of disulfonylchloride, 1.98 g of the chloride resulted (yield 79.1% of theoretical). M.p. 155-156° (according to Sivolobov), d_4^{20} 1.1639.

Found %: Cl 55.80, 55.89. $C_4H_8Cl_2$. Calculated %: Cl 55.90.

For the determination of structure, 1 g of the obtained dichloride was dissolved in 20 ml of alcohol, and 3 g of potassium rhodanide was added to the solution. The mixture was boiled on reflux for 40 hours on a water bath. After dilution of the mixture with water, the dirhodanide was extracted with ether, and after removal of the ether and alcohol traces on a water bath, the residue was suspended in 20 ml of water and treated with chlorine as described above. The chloranhydride precipitated during the reaction in the form of white flakes. From the melting point (81-82°) and by absence of depression, the identity with the chloranhydride of butanesulfonic-1,4-acid was established.

The Dichloranhydride of Butanedisulfonic-1,3-acid. Decomposition of the dichloranhydride and treatment of the dichloranhydride was carried out similarly to that described above for the 1,4-isomer. 1.15 g of the dichloride resulted (yield 72.5%) from 3.2 g of the dichloranhydride of butanedisulfonic-1,3-acid. B.p. 130-132° (according to Sivolobov), d_4^{20} 1.0849.

Found %: Cl 55.74, 55.62. $C_4H_8Cl_2$. Calculated %: Cl 55.90.

For determination of structure, 0.5 g of the obtained dichloride was converted into the disulfonylchloride in the same manner as with the preceding case. An oil resulted, which crystallized upon standing. Upon recrystallization from benzene and petroleum ether mixture, white needles resulted with a m.p. of 42-43°. The sample of the obtained dichloranhydride, mixed with initial dichloranhydride of butanesulfonic-1,3-acid did not show depression.

The Chloranhydride of Ethylbenzenesulfonic-1^2-acid. Decomposition of the chloranhydride was carried out in a manner similar to that described above for the dichloranhydrides of butanesulfonic acids. The chloride resulting upon decomposition was subsequently washed with sulfuric acid (d. 1.84) and then with water and dried with calcium chloride. 2.92 g of chloride resulted (59.4% of theoretical) from 7.15 g of the chloranhydride.

Found %: Cl 24.88, 24.96. C_8H_9Cl. Calculated %: Cl 25.56.

For structure determination the obtained chloride was subsequently converted into the rhodanide and sulfonyl chloride, in a manner as above. 0.48 g of sulfonyl chloride resulted from 2.1 g of the chloride. The former, after recrystallization from petroleum ether, had a m.p. of 81-82°. A test of the obtained chloranhydride when mixed with the initial chloranhydride did not show depression.

SUMMARY

L. It has been demonstrated that chlorides result from the thermal decomposition of paraffinic sulfonylchlorides (with yield 75-84%), wherein halogen takes the place of the sulfonyl group. The following were taken as objects for investigation: the chloranhydrides of propanesulfonic-2-acid, butanesulfonic-1-acid, 2-methylpropanesulfonic-1-acid, ethylbenzenesulfonic-1^8-acid and dichloranhydrides of butanesulfonic-1,4- and butanesulfonic-1,3-acids.

2. It has been recommended that the fatty sulfonyl chlorides be converted into the corresponding amides by treatment of ether solutions of the chloranhydrides with liquid ammonia. Amides are obtained with yields 90% of theoretical.

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SULFOCHLORINATION

II. ORIENTING EFFECT OF THE SO_2Cl AND Cl GROUPS DURING PHOTOCHEMICAL SULFOCHLORINATION

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In a preceding article by the authors [1], a brief review of contemporary methods for derivation of alkanesulfonyl chlorides, along with proposed methods for the identification and determination of sulfonyl group positions, was given. The latter consists of converting the sulfonyl chlorides into chlorides by heat; at such time, chlorine replaces the sulfonyl group. In the present article the authors have undertaken the task of clarifying certain problems related to the photochemical sulfochlorination process. Up to the present time, the theory on this process has received but little study. As is known, paraffinic hydrocarbons, when reacted with a mixture of sulfur dioxide and chlorine, with exposure to light of short wave length, convert into the chloranhydrides of the sulfonic acids with good yields; at the same time, direct chlorination also proceeds. In the first case it is obviously quite important to know what influence chlorine, entering into the hydrocarbon molecule, has upon introduction of the SO_2Cl group, and on the other hand, how the presence of the SO_2Cl group affects entry of chlorine, or of the second SO_2Cl group, into the molecule.

For elucidation of the first problem, the authors sulfochlorinated 1-chlorbutane. There resulted from the sulfochlorination a mixture of the chloranhydrides of chlorbutanesulfonic acids, from which it was difficult to isolate the individual isomers. To separate and to identify the resulting isomers, a method of thermal decomposition was investigated by the authors, and used. A mixture of butane dichlorides was obtained, which was converted into a mixture of disulfonychlorides (via the rhodanides), which was then separated by crystallization. There was isolated from 14.77 g of butanedisulfonylchloride mixture 3.45 g of the 1,4-isomer and 10.38 g of the 1,3-isomer, which were identified by their melting points. The first one had a m.p. of 83-84°, the second 40-41°. Isomers 1,1- and 1,2- were not found in noticeable quantities. Thus it is important to recognize that during the photochemical chlorination of chlorides, the entering SO_2Cl group is replaced by chlorine.

To investigate the effect of an SO_2Cl group upon entry of a second SO_2Cl group into the molecule, the chloranhydrides of butanesulfonic-1 and propanesulfonic-2 acids were photochemically sulfochlorinated. The sulfochlorides resulted from the corresponding chlorides by conversion to the rhodanides, with subsequent treatment of the latter by chlorine [2]. The chloranhydride of butanesulfonic-1-acid gave two dichloranhydrides: butanedisulfonic-1,4 and butanedisulfonic-1,3 acids. The chloranhydride of propanesulfonic-2 acid did not react with a mixture of chlorine and sulfur dioxide during six hours, with exposure to a mercury lamp. Thus, as with the chlorine atom, the SO_2Cl group also inhibit entry of a new SO_2Cl group into positions 1,1 and 1,2.

During the sulfochlorination of butanesulfonic-1 acid chloranhydride, there was separated, along with the dichloranhydrides, at this time, only two isomers: the chloranhydrides of 1-chlorbutanesulfonic-4 and 2-chlorbutanesulfonic-4 acid, i.e., the presence of the SO_2Cl group inhibits entry of the chlorine atom at the two carbon atoms nearest the SO_2Cl group. This deduction was also confirmed during the photochemical chlorination of butanesulfonic-1 acid chloranhydride, and in this case the chloranhydrides of 4-chlorbutanesulfonic-1 and 3-chlorbutanesulfonic-1 acid were obtained.

These simplest examples have indicated that during the photochemical processes, Cl and SO_2Cl, when present in the molecule, show a similar effect: they repel the second entering substituent (Cl or SO_2Cl); isomers 1,1 and 1,2 were not formed in noticeable quantities. Thus the chloranhydrides of sulfonic acids differ sharply from the haloanhydrides of the carboxylic acids. During chlorination of the chloranhydrides of butyric acid, the chloranhydride of α-chlorbutyric acid is formed, as was demonstrated by Markovnikov [3].

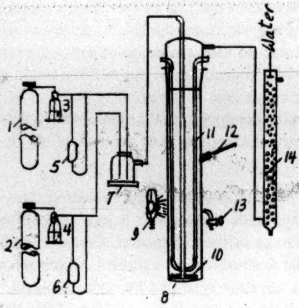
The bromination reaction of carboxylic acids in the presence of red phosphorous was studied in more detail by N. D. Zelinsky [4], through the formation of bromanhydrides. In this case bromine replaces the hydrogen atom at the α-carbon atom, even when the tertiary carbon atom is not in the α-position of the molecule. Thus, for example, α-bromisovaleric acid is formed from isovaleric acid, and from isocaproic acid is formed α-bromisocaproic acid. Upon chlorination of the free acids in the absence of phosphorous, this mechanism is not observed.

Thus, with chlorination of isovaleric acid in light, the β-chlorisovaleric acid [5] is formed, i.e., chlorine enters at the tertiary carbon atom, even though the latter is not in the α-position.

This peculiarity of the haloanhydrides of a carboxylic acid is explained by the fact that the latter, in distinction to the free acids, have a keto-enolic equilibrium shifted to the side of the enolic form. As is known, the sulfonic acids and their derivaties (but not the sulfones) have even less tendency to enolization than the carboxylic acids. To a certain degree this fact may serve as an explanation of the mechanism described above for the sulfochloride reaction.

EXPERIMENTAL

The reaction was carried out in Reactor 8 (see Figure). For gas feed the reactor was equipped with a tube ending in a porous plate. Temperature of the reaction mixture was controlled by thermometer 12, and was regulated by the supply of hot or of cold water in the U-shaped tube 11. Chlorine and sulfur dioxide were fed from tanks 1 and 2 through drying flasks 3 and 4 (filled with sulfuric acid) through mixer 7. The gas volumes were measured, respectively, by calibrated gasometers 5 and 6, illumination of the reaction mass being effected by a mercury lamp SVD Sh-250.



Distance between the lamp and the reactor was 30 cm. The outgoing gases were absorbed in column 14 by water.

Sulfochlorination of 1-Chlorbutane. Gaseous chlorine and sulfur dioxide were fed into 134.0 g of 1-chlorbutane (b.p. 77-78°; d_4^{20} 0.8869) for 7 hours, with exposure to a mercury lamp. Chlorine was fed in at a rate of 1.1 ml/sec.; SO_2 at a rate of 2.2 ml/sec. At first the reaction mass became colored greenish-yellow. After 30 minutes the mixture lost its color, and the temperature rose to 40°. After termination of the reaction, the mixture was flushed out with nitrogen. The increased weight after completion of the operation was 50.4 g. From a water bath 82.27 g of unreacted chlorbutane was distilled out from the reaction product. The residue was distilled in vacuo.

Fraction I, up to 70° (2.5 mm), 9.61 g, did not contain hydrolyzable chlorine and was not analyzed in detail, (probably di- and poly-chlorbutanes).

Fraction II, 105-116° (2.5 mm), 88.44 g.

Found %: Cl (sapon.) 18.51, 18.58. Cl (total) 37.16, 37.11. $C_4H_8O_2S_2Cl_2$. Calculated %: Cl (sapon.) 18.58; Cl (total) 37.17.

14.85 g of a mixture of dichlorbutanes resulted (b.p. 130-155°) from 31.48 g of Fraction II, upon thermal decomposition. 8.77 g of the dichlorbutanes was dissolved in 80 ml of ethyl alcohol, and to the solution was added 14.0 g of potassium rhodanide; the mixture was boiled for 40 hours on a water bath with a reflux condenser. After termination of reaction, 300 ml of water was added to the mixture, the rhodanide separated and was extracted with ether. After removal of the ether, the rhodanide was suspended in water and treated with gaseous chlorine to the appearance of a yellow coloration, which indicated excess chlorine. The latter was blown off with nitrogen. The chloranhydride formed separated in the form of a heavy, viscous oil, which solidified upon standing. The oil was extracted with ether, the ether solution was washed with water and dried with calcium chloride. After distilling off the ether, 14.77 g of residue resulted. The latter was dissolved in 10 ml of benzene, and to the solution was added 20 ml of carbon tetrachloride. 3.45 g of white needle crystals separated; after recrystallization from benzene and carbon tetrachloride, m.p. was 83-84°.

Found %: Cl (sapon.) 27.85, 27.77. $C_4H_8O_2S_2Cl_2$. Calculated %: Cl (sapon.) 27.84.

The crystals were identified as the chloranhydride of butanedisulfonic-1,4 acid from the melting point.

20 ml of petroleum ether was added to the filtrate resulting after separation of the chloranhydride of butanedisulfonic-1,4 acid. After standing, 10.38 g of white needle crystals separated out. After recrystallization from benzene and petroleum ether, m.p. was 40-41°.

Found %: Cl (sapon.) 27.80, 27.79. $C_4H_8O_4S_2Cl_2$. Calculated %: Cl (sapon.) 27.84.

The crystals were identified as the chloroanhydride of butanedisulfonic-1,3 acid from the melting point. Therefore Fraction II represented a mixture of two isomeric chloroanhydrides of 1-chlorobutanesulfonic-4 and 1-chlorobutanesulfonic-3 acids in the ratio of 1:3, judging from the quantity of disulfonic acid chloroanhydrides formed.

Sulfochlorination of Propanesulfonic-2-acid Chloroanhydride. A mixture of gaseous chlorine and sulfur dioxide was passed into 10.0g of the chloroanhydride of propanesulfonic-2 acid for 6 hours, with exposure to a mercury lamp. Chlorine was passed in at the rate of 0.3 ml per sec, SO_2 at 0.6 ml per sec. At first the reaction mass was colored yellowish-green, and it did not decolorize for the duration of the reaction period. Weight of the reaction mass after blowing through with nitrogen was 38.2 g. The reaction product was fractionally distilled under vacuo and all of it distilled at 71-72° (13 mm); d_4^{20} 1.2652.

Found %: Cl (sapon.) 24.82, 24.88. $C_3H_7O_2SCl$. Calculated %: Cl (sapon.) 24.91.

Consequently, the chloroanhydride of propanesulfonic-2 acid remained unchanged.

Sulfochlorination of the Chloroanhydride of n-Butanesulfonic-1-acid. Gaseous chlorine and sulfur dioxide mixture was fed into 126.0 g of the chloroanhydride of butanesulfonic-1 acid for 10 hours with exposure to light. Chlorine was supplied at the rate of 0.83 ml/sec, SO_2 at 1.23 ml/sec. The yellow-green color that appeared at the start disappeared after 20 minutes. Reaction temperature was maintained at 30-35°. After blowing nitrogen through the reaction mass, the weight increase constituted 47.0 g. Upon heating the reaction product in an oil bath (100-120°) at 2 mm, 119.3 g was distilled off, residue remaining in the distilling flask being 50.8 g. The volatile portion was fractionally distilled.

Fraction I, 77-79° (8 mm) —31.4 g.
Found %: Cl (sapon.) 22.58, 22.63. $C_4H_9O_2SCl$. Calculated %: Cl (sapon.) 22.68.
Fraction II, 107-111° (8 mm) —79.5 g.
Found %: Cl (sapon.) 18.53, 18.52; Cl (total) 37.08, 37.11. $C_4H_8O_2SCl$. Calculated %: Cl (sapon.) 18.58; Cl (total) 37.17.

10.4 g of Fraction II was thermally decomposed. 4.79 g (yield 69.1%) of dichlorobutane mixture resulted.

Found %: Cl (total) 55.73, 55.81. $C_4H_8Cl_2$. Calculated %: Cl (total) 55.90.

3.0 g of dichlorobutanes was dissolved in 40 ml of alcohol, 7.0 g of potassium rhodanide was added and the mixture was boiled for 40 hours on a reflux. After addition of water, the rhodanide separated and was extracted with ether. After distilling off the ether, 20 ml of water was added to the remainder and the mixture was chlorinated. The aqueous emulsion was saturated with gaseous chlorine while stirring. The chloroanhydride formed was extracted with ether and dried with calcium chloride. After removal of the ether, 4.31 g of viscous oily liquid resulted, which did not solidify upon prolonged standing. The oil was dissolved in 5 ml of benzene and 10 ml of carbon tetrachloride was added to the solution. Upon standing, 0.32 g of white needle crystals separated, which were again recrystallized from benzene and carbon tetrachloride mixture, m.p. 83-84°. The sample mixed with the chloroanhydride of butanedisulfonic-1,4 acid did not show depression.

10 ml of petroleum ether was added to the filtrate from the preceding operation. Upon standing, 3.38 g of white needle crystals with m.p. 40-41° separated, A sample mixed with the chloroanhydride of butanedisulfonic-1,3 acid did not show depression of melting point. Consequently, Fraction II represented a mixture of the chloroanhyrides of 3-chlorobutanesulfonic-1 and 4-chlorobutanesulfonic-1 acids.

The residue from the distillation, which solidified to a brown crystalline mass, was dissolved in 50 ml of benzene and boiled with activated charcoal to decolorize. 100 ml of carbon tetrachloride was added to the filtrate. Upon standing, white needle crystals separated out (31.6 g). After repeated crystallizations, m.p. was 83-84°, which corresponded to the melting point of butanesulfonic-1,4 acid chloroanhydride. 100 ml of petroleum ether was added to the filtrate from the 1,4-isomer. Upon standing, 15.3 g of white needle crystals separated out with a m.p. of 40-40.5°, corresponding to the butanedisulfonic-1,3 acid chloroanhydride.

Chlorination of Butanesulfonic-1-acid Chloroanhydride. Chlorine was fed into 100.0 g of butanesulfonic-1 acid chloroanhydride, with exposure, for 8 hours, at the rate of 0.5 ml per sec. The reaction temperature was maintained at 30-35°. After blowing off with nitrogen, the increased reaction mass weight was 14.9 g. The product was fractionally distilled in vacuo:

Fraction I, b.p. 79-82° (9 mm) −32.74 g; d_4^{20} 1.2069.

Found %: Cl (sapon.) 22.71, 22.68.

Fraction II, b.p. 100-112 (2 mm) −81.4 g.

Found %: Cl (sapon.) 18.57, 18.63; Cl (total) 37.10, 37.24. $C_4H_8O_2SCl_2$. Calculated %: Cl (sapon.) 18.58; Cl (total) 37.17.

For determination of composition, 20.0 g of Fraction II was thermally decomposed. 9.20 g of isomeric dichlorobutanes resulted, boiling in the range 128-157° (754 mm). 8.4 g of dichlorobutanes obtained was converted into a mixture of dichloroanhydrides, proceeding as above. 11.8 g of dichloroanhydrides mixture resulted. From the mixture, by subsequent precipitation, first with carbon tetrachloride and then with petroleum ether, the following resulted:

a) 2.7 g of the chloroanhydride of butanedisulfonic-1,4-acid, m.p. 83.5°.
Found %: Cl (sapon.) 27.73, 27.78. $C_4H_8O_4S_2Cl_2$. Calculated %: Cl (sapon.) 27.84.

b) 7.8 g of the chloroanhydride of butanedisulfonic-1,3-acid, m.p. 39.5-40.5° Found %: Cl (sapon.) 27.81, 27.69. $C_4H_8O_4S_2Cl_2$. Calculated %: Cl (sapon.) 27.84.

SUMMARY

The mechanism of Cl and SO_2Cl entry during the photochemical sulfochlorination reaction of hydrocarbons has been studied, as well as the influence of substituted groups already present in the molecule.

1-Chlorobutane, upon sulfochlorination, gave a mixture of isomeric chloroanhydrides of 4-chlorobutanesulfonic-1 and 3-chlorobutanesulfonic-1 acids in a ratio of approximately 3:1. Isomers 1,1 and 1,2 were not found.

During sulfochlorination of butanesulfonic-1 acid, the second SO_2Cl group enters only at position 4 and 3. Chlorination, which proceeds simultaneously, leads to exchange of the hydrogen atoms for chlorine in positions 4 and 3.

Under normal conditions of photochemical sulfochlorination, the chloroanhydride of propanesulfonic-2 acid remains unchanged.

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* See Consultants Bureau English translation, page. 209.

THE ESTERIFICATION MECHANISM OF GLUTARIC ACID

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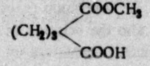
Only indirect methods are described in the literature for the synthesis of monomethylglutarate: by the method of methyl alcohol addition to the anhydride of glutaric acid [1], and as the result of acidolysis of dimethylglutarate with glutaric acid [2]. Attempts to synthesize monomethylglutarate by direct esterification of glutaric acid are as yet unknown. However, the following data are indicative of the feasibility of this method: 1) esterification conditions are close to acidolysis conditions; 2) the difference in hydrolysis constants for the glutaric acid carboxyls is quite significant ($K_1 = 0.1526$, $K_2 = 0.3940$).

Moreover, sebacic acid, the saponification constants of whose esters are approximately the same as for glutaric acid esters, according to the data of Adams [3], can be converted into the monomethyl ester by direct esterification. All of this, therefore, has preconditioned the attempted direct synthesis of monomethylglutarate by esterification of glutaric acid, avoiding intermediate stages.



$$(CH_2)_3\begin{cases} COOCH_3 \\ COOH \end{cases}$$

Esterification experiments with glutaric acid, using various quantities of methanol in the presence of H_2SO_4, indicated that only dimethylglutarate is formed as the principal reaction product.

The effect of various solvents was also studied, among them those which differentiated the esterification course of glutaric acid. A mixture of 50 g of glutaric acid and 15 g of methanol (1:1) was dissolved in the appropriate solvent and heated on a water bath. The experimental results are summarized in Table 1.

TABLE 1

Expt. No.	Solvent	Quantity of H_2SO_4 (ml)	Duration of heating (hrs)	Yield of dimethylglutarate (%)	Yield of monomethylglutarate (%)
23	Acetone (125 ml)	5	1	31	–
24		5	4	26.6	13.6
25	Acetone (125 ml)	5	6	23.3	16.5
26		5	13	22.5	16.9
27	Dichloroethane (100 ml) . . .	–	13	20.0	–
28		5	13	36.6	–
29	Dichloroethane (50 ml + acetone (50 ml)	–	13	16.6	–
30		5	13	41.6	12.7
31	Chloroform (100 ml)	–	13	16.0	–
33		5	13	55.0	–

Thus, esterifications of glutaric acid carried out in a medium of differentiating solvents, in the presence of catalyst (Experiments 23-26), and with their mixtures (Expt. 30), has resulted in the formation of small amounts of the acid ester. In the absence of catalyst, glutaric acid forms small amounts of the diester when in chloroform medium, and dichloroethane does not react at all in an acetone medium.

In order to improve reaction conditions, experiments were set up for the direct esterification of glutaric acid without catalyst (H_2SO_4).

TABLE 2

Expt. No.	Ratio of acid to alcohol quantities	Heating time	Yield	
			Mono- and dimethyl-glutarate (%)	Dimethyl-glutarate (%)
12	1.1	5	43.6	13.3
13	1:1.5	5	22.2	33.5
14	1:2	5	26.0	54.6
15	1:2.5	5	7.3	66.6
16	1:3	5	2.7	73.3
17	1:1	2.5	31.8	19.1
18	1:1	4.0	36.8	17.0
19	1:1	6.0	49.0	10.0
36	1:1	10.0	60.0	3.6
20	1:1	13.0	69.0	Traces
38	1:1	20.0	67.9	–

TABLE 3

Expt. No.	Diester and acid ratio (in moles)	Heating time (in hrs)	Quantity (in %)	
			Diester	Monoester
1	1:1	1.5	34.6	43.6
2	1:1	5.0	33.0	46.9
3	1:1	10.0	24.0	58.2
4	1:1	13.0	15.3	67.2
9	1:1	17.0	12.2	66.2

Preliminary experiments gave positive results immediately. Upon heating an equimolecular mixture of glutaric acid and methanol on an oil bath at 145-150° for 2 hours, a light-brown mass resulted, of sharp odor, containing 29.5% acid ester and 21.6% dimethylglutarate.

The experiments that followed clarified optimum reaction conditions, the most efficient ratio of initial substances – alcohol and glutaric acid, and also the relation of ester yields to reaction time. The results of these experiments are summarized in Table 2.

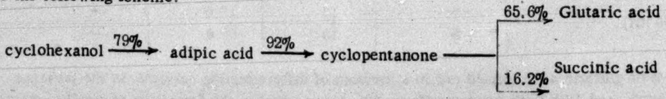
Consequently, direct esterification of glutaric acid by alcohol in the absence of H_2SO_4 catalyst leads to monomethylglutarate as the principal reaction product, while with an increase in the heating time of an equimolecular mixture, the acid ester yield is increased, and stabilizes after 13 hours of heating, while the content of dimethyl ester in the reaction mixture decreases. This brings to mind a thought that monomethylglutarate formation during the direct esterification of glutaric acid by alcohol is realized through an intermediate formation of dimethylglutarate, with its subsequent acidolysis by glutaric acid. To confirm this assumed formation mechanism for the glutaric acid ester, the authors carried out dimethylglutarate acidolysis experiments in relation to time. As a result of these experiments (Table 3) it was found that the most complete acidolysis occurs with equimolecular quantities of dimethylglutarate and glutaric acid. As experiments carried out under the same conditions as with esterification of glutaric acid were increased in time, the extent of acidolysis increased, and the dimethyl ester converted into monomethylglutarate, forming a mixture of unreacted diester and of monomethylglutarate after 13 hours heating.

Increase in experiment time to 17 hours has almost no effect upon the yield of monoester.

Thus, the experiments given in Table 3 confirm the authors' assumption concerning the fact that direct esterification of glutaric acid, as carried out by the authors, proceeds in two stages; the dimethyl ester formed during progress of the acid esterification enters into reaction with a second molecule of glutaric acid, forming monomethylglutarate.

EXPERIMENTAL

Glutaric Acid Synthesis. The glutaric acid was synthesized by a method developed by Markovnikov, with addition of precise specifications made by other scientists [4,5,6,1]. Synthesis was carried out according to the following scheme:



The mixture of glutaric and succinic acids resulting from oxidation of cyclopentanone was separated. In place of the orthodox, but complicated separation method for these acids by means of conversion to the barium salts, the authors utilized a sharp difference in solubility of glutaric and succinic acids in benzene.

1.42 kilograms of the acid, with m.p. 95-97°, resulted from 2.3 kilograms of cyclopentanone.

Esterification of Glutaric Acid. All experiments on esterification of glutaric acid and acidolysis of the dimethylglutarate were carried out in the same manner; a solvent and H_2SO_4 catalyst were added (Table 1) and the reaction mixture was heated in a round-bottomed flask with a reflux condenser on a boiling water bath. The glutaric acid esterification experiments without solvents, and the acidolysis, were carried out with heating to 145-150° on an oil bath. The reaction mass, heated through, was cooled and the flask contents were transferred to a Claison flask with fractionating column. After distilling off the solvent and alcohol, the residue on the water bath was fractionally distilled in vacuo. Fraction I, collected at 108-112° (23 mm), corresponded to dimethylglutarate. Fraction II, collected at 158-163° (23 mm) consisted principally of monomethylglutarate. Repeated fractional distillations of the ester fractions from several experiments indicated that Fraction 1 contained dimethylglutarate of sufficiently high purity.

The ester fraction (158-163°) was contaminated with 2-5% of glutaric acid, easily removable by repeated distillations in vacuo. Here the resulting product obtained boiled at 165-166° (23 mm).

d_{21} 1.1740; n_D^{21} 1.4419; MR_D 32.8908; calculated 33.0980.

SUMMARY

1. A method of monomethylglutarate synthesis has been developed by means of direct esterification of glutaric acid with methanol, in yields up to 69% of theoretical.

2. The effect of initial mixture composition, time of reaction, H_2SO_4 catalyst, and of solvents upon esterification of glutaric acid have been studied.

3. A reaction mechanism for monomethylglutarate formation by direct esterification of glutaric acid has been proposed. The reaction proceeds in two stages: at first dimethylglutarate is formed, which then, by acidolysis, is converted to the monomethyl ester of glutaric acid.

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COMPARATIVE HYDROGENATION OF UNSATURATED FATTY ACIDS C_{16}, C_{18} and C_{22}

P. A. Artamonov

As a development of the problem which was touched upon by the author in regard to the hydrogenation kinetics of unsaturated fatty acids [1,2], the author in the present investigation has undertaken the task of clarifying the effect of the carbon chain length upon the magnitude of the hydrogenation rate.

As objects for study, the unsaturated fatty acids, of general formulas $C_{16}H_{30}O_2$, $C_{18}H_{34}O_2$ and $C_{22}H_{42}O_2$, were selected, obtained partially by synthetic means, and partially by isolation from natural vegetable oils. Comparative hydrogenation experiments for the following pairs of unsaturated fatty acids were carried out: 1) hexadecene-2-acid-1 and octadecene-2-acid-1; 2) octadecene-2-acid-1 and docosene-2-acid-1; 3) octadecene-9-acid-1 and docosene-13-acid-1. Certain constants for these acids are given in Table 1.

TABLE 1

No.	Acid names	M	M.p.	Iodine No. according to Guble
1	Hexadecene-2-acid-1	254.24	49.0*	26.3*
2	Octadecene-2-acid-1	282.27	59.0	21.1*
3	Docosene-2-acid-1	338.34	68.5	18.75*
4	Octadecene-9-acid-1	282.27	14.2	89.3
5	Docosene-13-acid-1	338.34	33.5	74.38

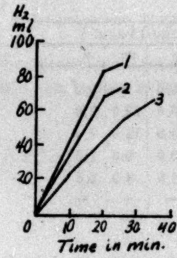

Fig.1. 1) Hexadecene-2-acid-1; 2) octadecene-2-acid-1, 3) docosene-2-acid-1.

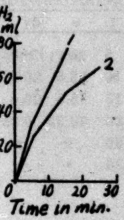

Fig.2. 1) Octadecene-9-acid-1; 2) docosene-13-acid-1.

Hydrogenation was carried out with electrolytic hydrogen in dry diethyl ether at room temperature. Palladium black was used as a catalyst, obtained by the method of Willstätter. In the course of the experiments, the author used one and the same sample of catalyst and solvent in order to eliminate possible effects of the conditions of their preparation on the course of hydrogenation. For obtaining comparative data, hydrogenation was carried out on acid pairs. The experimental procedure was as follows: the investigated pairs of acids were placed together with the solvent into two glass containers (15 ml of an ester solution of the analyzed acids, 0.263 molar), set up in an apparatus for shaking, and connected with two burets filled with hydrogen such that each buret with container for hydrogenation constituted a closed cycle. The shaking device was set into movement by an electric motor. After defined time intervals, the hydrogen consumed was measured. The volume of absorbed hydrogen was brought to 0° and 760 mm pressure. The hydrogenation rate constant was calculated by an equation of zero order.

EXPERIMENTAL

1. Comparative Hydrogenation of Hexadecene-2-acid-1 and Octadecene-2-acid-1. The investigated acids were obtained by treatment of α-bromopalmitic acid and α-bromostearic acids with an alcoholic potassium hydroxide solution, using the methods described in the preceding works [1,3] by the author. Hydrogenation was carried out at a temperature of 22° and 760.5 mm. Experimental results of the hydrogenation are given in Table 2.

t = time (in minutes); v = volume of absorbed hydrogen (in milliliters), brought to 0° and 760 mm; dv = volume (in ml) of hydrogen absorbed within the time measured; k = quantity of hydrogen absorbed in one minute.

From the data of Table 2 it can be seen that hexadecene-2-acid-1 hydrogenates more rapidly than octadecene-2-acid-1. However, upon comparing the hydrogenation rates of octadecene-2-acid-1 and decosene-2-acid-1 (Table 3) it can be seen that octadecene-2-acid-1 in its turn hydrogenates more rapidly than decosene-2-acid-1.

* Lowered iodine numbers are characteristic for α- and β-unsaturated acids [3].

2. Comparative Hydrogenation of Octadecene-2-acid-1 and Docosene-2-acid-1. The docosene-2-acid-1 necessary for the experiments was obtained by the author through a splitting off of the bromine from *a*-bromobehenic acid, using alcoholic alkali and heat [4]. The experimental results of hydrogenation are given in Table 3, and the course of the hydrogenation curves for the investigated acids is presented in Fig. 1.

TABLE 2

Hexadecene-2-acid-1				Octadecene-2-acid-1			
t	v	dv	k	t	v	dv	k
5	25	20	5.0	5	21.3	–	4.26
10	45	19.7	4.0	10	38.0	16.7	3.34
15	64.7	19.1	3.94	15	53.0	15.0	3.0
20	83.8	4.0	3.82	20	68.0	15.0	3.0
25	87.8	–	0.8	25	74.0	6.0	1.2

TABLE 3

Octadecene-2-acid-1				Docosene-2-acid-1			
t	v	dv	k	t	v	dv	k
5	21.4	17.0	4.28	5	14.0	–	2.80
10	38.4	16.4	3.4	10	25.5	11.5	2.30
15	54.8	16	3.28	15	35.5	10.0	2.00
20	70.4	4.5	3.20	20	44.75	9.25	1.85
25	75.3	–	0.9	25	53.75	9.0	1.85
–	–	–	–	30	60.75	7.0	1.40
–	–	–	–	35	66.25	55.	1.10

TABLE 4

Octadecene-9-acid-1				Docosene-13-acid-1			
t	v	dv	k	t	v	dv	k
5	35	–	7.0	5	25.0	–	5.0
10	55.5	20.5	4.1	10	38.0	13.0	2.6
15	75.5	20.0	4.0	15	50.0	12.0	2.4
20	76.35	0.85	0.17	20	59.0	9.0	1.8
25	–	–	–	25	67.0	8.0	1.6
30	–	–	–	30	–	–	–

Analysis of the resulting data (Tables 2, 3 and Fig. 1) indicates that the size of the fatty acid molecule evidently affects the hydrogenation course, namely, the longer the carbon chain length for the unsaturated fatty acid molecule, the slower the addition of hydrogen at the double bond proceeds.

Of the three acids investigated by the author, docosene-2-acid-1, with 22 carbon atoms in its molecule (M = 338.34), hydrogenates the slowest, and hexadecene-2-acid-1 with 16 carbon atoms in its molecule (M = 254.24) hydrogenates the fastest.

3. Comparative Hydrogenation of Octadecene-9-acid-1 and Docosene-13-acid-1. Of interest to the author was the problem: is the above-mentioned mechanism preserved between the unsaturated fatty acid molecular weight and its hydrogenation rate if fatty acids with different double bond positions from the carboxyl group are taken, than the *a*-unsaturated acids which were taken for investigation by the author. To solve this problem, a comparative hydrogenation of octadecene-9-acid-1 (oleic acid) and docosene-13-acid-1 (erucic acid) was carried out. The acids necessary for the experiments were isolated from natural vegetable oils. Oleic acid was isolated from olive oil, and erucic from rape oil. Conditions of hydrogenation were the same as in the preceding cases. Experimental results are given in Table 4 and in Fig. 2.

It can be seen that here too is maintained the relation observed by the author between the unsaturated fatty acid molecular weight and its hydrogenation rate, namely: the longer the carbon chain length of the molecule, the slower does hydrogenation proceed. Docosene-13-acid-1 (erucic acid) hydrogenates considerably slower (1.5-2 times) than does octadecene-9-acid-1 (oleic acid). From this it is possible to explain the fact which is met everyday in practice that oils from the cruciferrae family (rape, mustard and colza), which contain large amounts (up to 50%) of erucic acid, hydrogenate considerably slower, as a rule, than sunflower, cotton and other oils, which are composed principally of the triglycerides of the unsaturated fatty acids C_{16} and C_{18}.

It is of interest to note that the rate of hydrogen addition to the double bond of an unsaturated fatty acid apparently depends, to a more considerable extent upon the carbon chain length of the molecule, than upon the carboxyl group position with respect to the double bond.

In the author's preceding work on a study of the hydrogenation rate of octadecene acids [1], it was established that as the double bond becomes farther removed from the carboxyl group, the rate of hydrogen addition to the double bond increases. Proceeding from this position, erucic acid, in which the double bond is in position 13-14 from the carboxyl group, should hydrogenate at a greater rate than oleic, whose double bond in the chain is considerably nearer (9-10) to the carboxyl group. However, as can be seen, the results are contrary, due to a higher molecular weight of erucic acid as compared with oleic acid. Consequently, the mechanism of hydrogen addition rate to unsaturated fatty acids in relation to the double bond position is apparently preserved only for acids of the same order.

SUMMARY

1. The rate of hydrogenation of unsaturated fatty acids decreases with an increase in molecular weight. Hexadecene-2-acid-1 hydrogenates more rapidly than octadecene-2-acid-1, and in its turn octadecene-2-acid-1 hydrogenates at a more rapid rate than docosene-2-acid-1.

2. The difficulty in hydrogenation of vegetable oils from the cruciferrae family (rape, mustard, and colza) which is encountered in practice is explained by the low hydrogenation rate of docosene-13-acid-1 (erucic acid) as compared with the hydrogenation rates of hexadecene and octadecene acids which enter into the composition of sunflower, cotton and other oils.

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* See Consultants Bureau translation, p. 1187.

** See Consultants Bureau translation, p. 2037.

*** See Consultants Bureau translation, p. 2041.

ALKYL ESTERS OF GLYCEROL

M. S. Malinovsky and V. M. Vvedensky

The present investigation was undertaken with the purpose of clarifying the influence of alcohol type upon its order of addition to glycides and the yield of glycerol monoester.

Methyl, ethyl, propyl, iso-propyl, n-butyl, iso-butyl, ter-butyl, n-amyl, iso-amyl, allyl and benzyl alcohols were taken. All of the alcohols mentioned form monoesters (some of them synthesized for the first time by the authors), and at the same time the following regularities were observed.

1) The normal primary alcohols give the highest yields (approximately 60-80%) of glycerol monoesters 2) Primary alcohols of iso-structure form monoesters in poorer yields than the normal alcohols. Thus, for example, the monoester yield for isobutyl alcohol was 29%, and for isoamyl 34%. 3) The secondary alcohols give monoesters, but not with such high yields, on the average 30-35%. 4) Tertiary alcohols, as was expected, gave the monoesters in poor yields (3-4%), and prolonged heating of their components is required, up to approximately 20 hours. 5) Benzyl alcohol reacts with glycide with more difficulty than with the secondary alcohols, and the monoester yield reaches 16-18%.

None of the synthesized glycerol esters mix with benzene, and apart from the methyl ester, they are insoluble in water. They mix with ethyl alcohol and acetone in all proportions. Monoesters with amyl, iso-amyl and allyl radicals are insoluble in ethyl ether. The boiling points and specific gravities of the monoesters are given in the Table.

In the reaction of alcohol with a glycide the formation of an α- or a β-form of the monoesters may be expected. The authors obtained only α-esters, identical in structure with the esters resulting from the α-chlorohydrin of glycerol and the alcoholates of the corresponding alcohols. Due to the fact that some of the glycerol monoesters described here have been synthesized for the first time by the authors, it was obligatory, for structure confirmation, to synthesize them from the alcoholates by the procedure indicated above; the esters in this case resulted in poor yields. Conformity of the ester constant synthesized from the glycide and the α-chlorohydrin of glycerol indicated that only the α-monoesters of glycerol result from glycides and alcohols.

The results obtained by the authors are in good agreement with the data of A. A. Petrov and M. G. Vladimirova [1]. The authors mentioned established that for the most part only α, γ-diesters are formed, i.e., that the oxide ring of glycide is open on the side of the tertiary carbon atom, which has likewise been observed by the present authors.

EXPERIMENTAL

Condensation of Glycide with Methyl Alcohol. Taken: 7.5 g (0.1 mole) of glycide, 16 g (0.5 mole) of methyl alcohol, and 1% of the mixture weight in concentrated sulfuric acid in the role of catalyst.

Sulfuric acid was added to the alcohol with cooling, and then the glycide in small portions. With such a mixing order for the components, the highest yield of the monoester resulted. If one proceeds, on the contrary, to mix alcohol with the glycide and then to add the acid, then each drop of the latter reacts very rapidly. The glycide oxide resinifies. Under the conditions indicated above, resinification was not observed, although the reaction proceeded with strong heat evolution, because of which the flask had to be well-cooled.

After termination of reaction, the sulfuric acid was neutralized with barium carbonate and the ether was distilled off in vacuo. 7.9 g of monoester resulted, which constituted 75%.

Repeated experiments have indicated that a two-fold or three-fold decrease in quantity of alcohol always decreases the monoester yield by 50%. A 0.1% decrease in quantity of acid also decreases the ester yield to a high degree; on the other hand, an increase in quantity of acid up to 2% increases the monoester yield up to 85%.

A further increase in the quantity of acid did not affect the ester yield.

TABLE

The Properties of Glycerol Monoesters

No.	Name of Ester	Formula	B.p. (731-736 mm)	d^{20}	Per cent OH groups	
					found	calculated
1	α-Methyl ester of glycerol[2]	$CH_3OCH_2CH(OH)CH_2OH$	198-200°	1.183	–	–
2	α-Ethyl ester of glycerol [3]	$C_2H_5OCH_2CH(OH)CH_2OH$	219-222	1.0947	–	–
3	α-Propyl ester of glycerol [4]	$C_3H_7OCH_2CH(OH)CH_2OH$	221-224	1,0826	–	–
4	α-Isopropyl ester of glycerol	$(CH_3)_2CHOCH_2CH(OH)CH_2OH$	187-190	1.0063	25.10	25.35
5	α-Butyl ester of glycerol	$C_4H_9OCH_2CH(OH)CH_2OH$	226-227	1.0585	22.65	22.95
6	α-Isobutyl ester of glycerol	$(CH_3)_2CHCH_2OCH_2CH(OH)CH_2OH$	216-218	1.0656	22.21	22.95
7	α-Ter-Butyl ester of glycerol	$(CH_3)_3COCH_2CH(OH)CH_2OH$	209-211	1.0764	22.40	22.95
8	α-Amyl ester of glycerol [5]	$C_5H_{11}OCH_2CH(OH)CH_2OH$	257-260	1.0663	–	–
9	α-Isoamyl ester of glycerol	$(CH_3)_2CHCH_2CH_2OCH_2CH(OH)CH_2OH$	248-250	1.0047	–	–
10	α-Allyl ester of glycerol	$H_2C{=}CHCH_2OCH_2CH(OH)CH_2OH$	209-210	1.0869	25.54	25.74
11	α-Benzyl ester of glycerol	$C_6H_5CH_2OCH_2CH(OH)CH_2OH$	274-276	1.0263	18.60	18.72

The ester which the authors have synthesized for the first time from glycide was obtained by heating sodium methylate with the α-chlorohydrin of glycerol [2].

The remaining esters given in the Table were synthesized in the same manner as the methyl ester, except that in certain instances the reaction mixture had to be heated on a water bath. In a majority of the cases, 2 hours of heating was quite adequate for maximum ester yield, and it was only the condensation of glycide with ter-butyl alcohol that required 20 hours of heating.

0.1 mole of glycide, 0.5 mole of the corresponding alcohol and sulfuric acid to the amount of 2% of the mixture weight were taken in all condensations.

The molecular weights of the synthesized esters were determined and the deviation between found and calculated data consisted of 1 to 3% for the hydroxyl group content.

The esters indicated in the Table under Nos. 5 , 8 and 10 were obtained, moreover, from the glycerol α-chlorohydrin by the method given in the literature.

SUMMARY

1. The condensation of glycide with various primary, secondary and tertiary alcohols has been investigated.

2. The mechanism of glycerol monoester formation from glycide and conditions for highest yields have been brought out.

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INVESTIGATION OF OLEFIN OXIDES

CONDENSATION OF OLEFIN OXIDES WITH PHOSGENE

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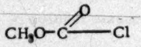
As is known, the chloroanhydride of carbonic acid, or phosgene, reacts readily with alcohols to form esters of chlorocarbonic acid. A second phosgene chlorine atom enters into reaction with excess alcohol and high temperature, which leads to the complete esterification of carbonic acid. In order to avoid this second reaction, strong cooling and considerable phosgene excess in relation to alcohol are necessary, which leads to variations in this reaction, namely: the alcohol can be reacted with liquid phosgene with strong cooling [1], or the alcohol can be dropped onto charcoal fragments saturated with phosgene [2].

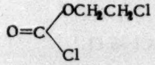
When phosgene and alcohol react, hydrogen chloride is usually evolved, which, upon dissolving in the liquid, shifts the equilibrium (for the first reaction) to the left, leading to decreased yields of chlorocarbonic esters. To avoid this reverse reaction, hydrogen chloride must be removed from the reaction medium, which is realized either by bubbling air through, or by addition of weak organic bases [3] (dimethylaniline, pyridine, antipyrine, and others), or by addition of marble. In the latter case water must also be introduced for solution of the calcium chloride which results from the reaction process.

Quite obviously the thought arose of carrying out the first reaction in such a manner as to have no worry concerning the formation of a full ester of carbonic acid, or the reverse process, which leads to decomposition of chlorocarbonic esters. For this purpose the authors made use of olefin oxides, which when reacted with phosgene should be completely added to the latter, as the result of which the need for fixing hydrogen chloride no longer arises.

During the reaction of phosgene with olefin oxides, chlorocarbonic esters, or the full esters of carbonic acid may be expected.

In reality it was found that reaction proceeds in the first direction, and even with a large excess of oxide the full ester of carbonic acid does not result. This was also confirmed by special experiments on the condensation of the readily-prepared ester of chlorocarbonic acid  $CH_3O-C(=O)-Cl$ with ethylene, propylene and epichlorhydrin oxides. Despite the fact that the oxide was passed into (or was added dropwise to) the above-indicated ester, which was heated on a water bath, condensation was not observed, and the ester remained unchanged.

The authors synthesized the following esters of chlorocarbonic acid from the olefin oxides: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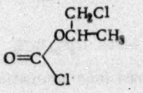
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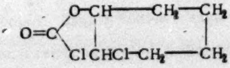
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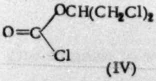
(IV)

The structure of these esters was confirmed by saponification, the result of which gave the corresponding chlorohydrins of the glycol. Furthermore, some of the above-mentioned esters are described in the literature (synthesized by other methods), and their constants coincide fully.

According to their odor , the chlorocarbonic acid esters are similar to the methyl ester of chlorocarbonic acid.

EXPERIMENTAL

Phosgene was obtained from carbon tetrachloride by reacting with oleum of high percentage [4].

The esters were synthesized as follows. The calculated quantity of cooled olefin oxide was slowly added to a solution of the determined quantity of phosgene in ethyl bromide. The reaction proceeded violently, and so the mixture was cooled with water and ice for the entire period. After introduction of the oxide the reaction mixture was left to stand overnight at 0°, and the solvent was then distilled off, the residue washed with ice water, dried with anhydrous sodium sulfate and redistilled.

An excess of phosgene does not impair the reaction, and it is better to take somewhat more of the latter than of olefin oxide. As solvents, benzene, toluene, carbon tetrachloride, dichloroethane, and others, may be taken, but best of all is ethyl bromide. The ethyl bromide has a low boiling point (+ 38°), and consequently is easily removable from the resulting chlorocarbonic acid ester and does not contaminate the latter. The other indicated solvents always contaminate the resulting chlorocarbonic ester and for its purification repeated distillations are required.

β-Chloroethyl Ester of Chlorocarbonic Acid (I). This product resulted in 50% yield from ethylene oxide and phosgene, and is a colorless liquid, b.p. 153°.

d_4^{18} 1.3760. Found %: Cl 50.08. $C_3H_4O_2Cl_2$. Calculated %: Cl 49.65.

This ester is described in the literature and was synthesized for the first time by the action of chlorine upon chlorcarbonic acid ethyl ester [5], together with the α-isomer, and also from ethylenechlorhydrin and phosgene [6]. According to the literature data, the ester has a b.p. of 152.5° and d_4^{20} 1.3825.

β-Chloroisopropylester of Chlorocarbonic Acid (II). This ester was obtained from propylene oxide and phosgene in 55% yield. A colorless liquid with b.p. 68-70° at 70 mm.

d_4^{18} 1.1610; n_D^{18} 1.44619.

0.2080 g substance: 0.3784 g AgCl. Found %: Cl 45.00. $C_4H_6O_2Cl_2$. Calculated %: Cl 45.22.

Upon heating the ester with an aqueous solution of potash, propylenechlorohydrin resulted, the presence of which confirms the written formula.

o-Chlorocyclohexyl Ester of Chlorocarbonic Acid (III). This ester resulted in 75-80% yield from cyclohexene oxide. A colorless liquid with b.p. 108-110° at 13 mm.

d^{18} 1.2158. 0.1938 g substance: 0.2798 g AgCl. Found %: Cl 35.73. $C_7H_{10}O_2Cl_2$. Calculated %: Cl 36.04.

When the ester was heated with an aqueous solution of potash, cyclohexene chlorohydrin resulted, which confirms the proposed formula.

β,β'-Dichloroisopropyl Ester of Chlorocarbonic Acid (IV). This ester resulted in 80% yield from epichlorohydrin and phosgene. B.p. 78-80° at 20 mm.

d^{20} 1.3736; n_D^{20} 1.4804.

0.1928 g substance: 0.4304 g AgCl. Found %: Cl 55.02. $C_4H_5O_2Cl_3$. Calculated %: Cl 55.61.

The ester is described in the literature; it was obtained from symmetrical dichloroisopropyl alcohol and phosgene [7].

SUMMARY

1. The chlorosubstituted chlorocarbonic esters may be synthesized successfully by reaction of phosgene with the corresponding olefin oxides.

2. The intermediate chlorinated esters of carbonic acid do not result from an interaction of phosgene and olefin oxides, which simplifies the purification of chlorinated esters of chlorocarbonic acid.

3. It is most expedient to condense the olefin oxide with phosgene in ethyl bromide solution which is readily removed and does not contaminate the principal reaction product.

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THE AMIDATION MECHANISM OF CARBOXYLIC ACIDS BY AMIDES OF SULFURIC ACID

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At the present time enough factual material has been accumulated to evaluate possible amidation mechanisms of carboxylic acids by sulfuric acid amides and to verify them experimentally. Acid amides [1] result during the sulfamide reaction with carboxylic acids, and with dimethylsulfamide only the acid dimethylamides result [2]:

$$RCOOH + NH_2SO_2NH_2 \rightarrow RCONH_2 + NH_2SO_2OH;$$

$$RCOOH + NH_2SO_2N(CH_3)_2 \rightarrow RCON(CH_3)_2 + NH_2SO_2OH.$$

Upon reacting diphenylsulfamide with carboxylic acids, the phenylamides of carboxylic acid result [3]:

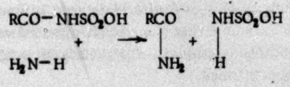
$$RCOOH + C_6H_5NHSO_2NHC_6H_5 \rightarrow RCONHC_6H_5 + C_6H_5NHSO_2OH.$$

All of these reactions can be very well explained if an amidation mechanism similar to the esterification mechanism described in one of our preceding works [1] is adopted. According to this mechanism, the presence of "free" hydrogen in sulfamide is not essential, and amidation should also proceed for quaternary substituted sulfamides. However, it was determined that carboxylic acids do not react with quaternary substituted sulfamides. Consequently, the amidation mechanism proposed earlier is also inaccurate.

Evidently one or two "free" hydrogen atoms in the sulfamide molecule are indispensable for the amidation reaction. It was found that the interaction of tri-substituted sulfamides with carboxylic acids proceeds readily, while in the case of asymmetrical dimethylphenylsulfamide, a mixture of dimethylamides and phenylamides results:

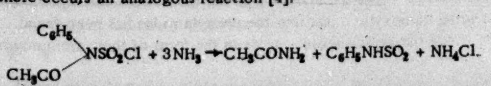
$$RCOOH + (CH_3)_2NSO_2NHC_6H_5 \rightarrow \underset{\sim 55\%}{RCON(CH_3)_2} \text{ and } \underset{\sim 30\%}{RCONHC_6H_5}.$$

Inasmuch as only one "free" hydrogen in the sulfamide is necessary and sufficient, it was therefore thought that the intermediate products were the acylsulfamides of acylamino acids ($RCONHSO_2NH_2$ or $RCONHSO_2OH$) which are further aminolyzed by ammonia or amines at the CN bond with amide and sulfamino acid formation:



$$\begin{matrix} RCO-NHSO_2OH \\ + \\ H_2N-H \end{matrix} \rightarrow \begin{matrix} RCO \\ | \\ NH_2 \end{matrix} + \begin{matrix} NHSO_2OH \\ | \\ H \end{matrix}$$

Aminolysis may proceed both intramolecularly and extramolecularly. The likelihood of such aminolysis is confirmed by the fact that during reaction of ammonia or amines with the chloranhydrides of aryl-acylsulfamino acids, there occurs an analogous reaction [4]:



$$\begin{matrix} C_6H_5 \\ CH_3CO \end{matrix}\!\!>\!NSO_2Cl + 3NH_3 \rightarrow CH_3CONH_2 + C_6H_5NHSO_2 + NH_4Cl.$$

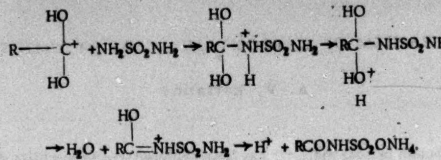
The hypothesis of N-S bond hydrolysis is eliminated because if this hypothesis were true, then the carboxylic acid dimethylamides could not result from amidation by asymmetrical dimethylsulfamides. For the same reasons, sulfanic acid ($N \equiv SOOH$) and isosulfanic acid ($NH = SO_2$) could not become active amidating agents. But isosulfanic acid may become a passive amidating agent, i.e., by removing water from ammonium or substituted ammonium salt.

This hypothesis seems to be somewhat artificial, but has not as yet been refuted experimentally. However, from the hypothesis we cannot draw the conclusions that were inferred (and experimentally confirmed) from the theory which assumes that the acyl sulfoaminic acids are formed as intermediate products.

The formation of acylsulfaminic acids can occur through two mechanisms: isosulfanic acid is formed as an intermediate product:

$$(CH_3)_2NSO_2NHC_6H_5 + C_6H_5N = SO_2 \xrightarrow{RCOOH} RCON(C_6H_5)SO_2OH,$$

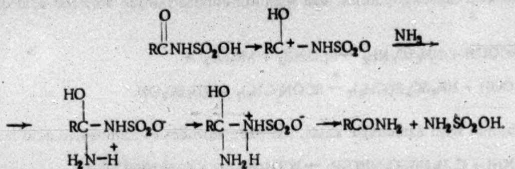
or, which is more probable, according to the mechanism which is similar to the esterification mechanism, but somewhat different from that earlier proposed [1], i.e., according to the scheme:



$$R-\overset{HO}{\underset{HO}{C^{+}}} + NH_2SO_2NH_2 \rightarrow R\overset{HO}{\underset{HO}{C}}-\underset{H}{\overset{+}{N}}HSO_2NH_2 \rightarrow R\overset{HO}{\underset{\underset{H}{HO^{+}}}{C}}-NHSO_2NH_2$$

$$\rightarrow H_2O + R\overset{HO}{C}=\overset{+}{N}HSO_2NH_2 \rightarrow H^{+} + RCONHSO_2ONH_4.$$

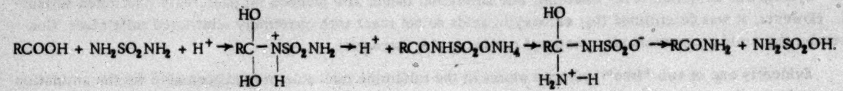
Aminolysis may proceed by the same scheme, i.e.:



$$R\overset{O}{\overset{\|}{C}}NHSO_2OH \rightarrow R\overset{HO}{C^{+}}-NHSO_2O \xrightarrow{NH_3}$$

$$\rightarrow R\overset{HO}{\underset{H_2\overset{+}{N}-H}{C}}-NHSO_2O^{-} \rightarrow R\overset{HO}{\underset{NH_2}{C}}-\underset{H}{\overset{+}{N}}HSO_2O^{-} \rightarrow RCONH_2 + NH_2SO_2OH.$$

Thus it is quite probable that amidation of carboxylic acid by sulfamides proceeds according to the following mechanism:



$$RCOOH + NH_2SO_2NH_2 + H^{+} \rightarrow R\overset{HO}{\underset{HO}{C}}-\underset{H}{\overset{+}{N}}SO_2NH_2 \rightarrow H^{+} + RCONHSO_2ONH_4 \rightarrow R\overset{HO}{\underset{H_2N^{+}-H}{C}}-NHSO_2O^{-} \rightarrow RCONH_2 + NH_2SO_2OH.$$

This mechanism explains all of the observed facts except one. If the proposed mechanism is correct, then only dimethylamide should result during interaction of dimethylphenylsulfamide with the carboxylic acid, whereas in actuality a mixture of both dimethylamides and phenylamides results. This nonconformity is explained by the fact that upon reacting the carboxylic acids with unsubstituted or asymmetric di-substituted sulfamide, sulfaminic acid is formed as a stable, highly difficult to hydrolyze, sulfaminic acid, and the reaction of carboxylic acids with dimethylphenylsulfamide results in an unstable side product, phenylsulfaminic acid, which is extremely easy to hydrolyze. This acid is well known in the form of salts, but no one as yet has apparently isolated it in the pure state. Buhner gives a m.p. above 280° for the phenylsulfaminic acid, and Wohl and Koch report that phenylsulfaminic acid melts at 77° [5]. A characteristic property of phenylsulfaminic acid is found to be the tendency for hydrolysis of the N-S bond; consequently it might be assumed that phenylsulfamic acid would be acidolyzed by carboxylic acids, with the formation of carboxylic acid phenylamides: $C_6H_5NHSO_2OH + RCOOH \rightarrow RCONHC_6H_5 + H_2SO_4$. This hypothesis was tested and experimentally confirmed.

The ammonium salt of phenylsulfamino acid was obtained by reacting sulfamino acid with aniline [6], and without purification was heated with p-nitrobenzoic acid in pyridine solution. From this the corresponding phenylamide resulted with a yield about 30% of theory. Thus the accuracy of the theoretical assumption was confirmed, and one more way of directly transforming carboxylic acids into the phenylamides has been found. It is possible that it will find practical application, since the arylsulfaminic acids in the form of their ammonium salts are cheap and easily accessible.

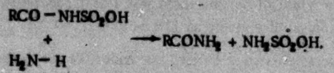
Formation of phenylamides from the phenylsulfoaminic acid and carboxylic acids was again confirmed by an additional experiment. A mixture of 2 moles of p-nitrobenzoic acid was heated in pyridine solution with 1 mole of phenylsulfamide. p-Nitrobenzanilide resulted in 73.6% yield by the following scheme:

$$2RCOOH + C_6H_5NHSO_2NHC_6H_5 \rightarrow 2RCONHC_6H_5 + H_2SO_4,$$

and in a yield of 147.2% of theory based upon calculation according to the scheme

$$RCOOH + C_6H_5NHSO_2NHC_6H_5 \rightarrow RCONHC_6H_5 + C_6H_5NHSO_2OH.$$

This can only be explained by the fact of phenylsulfaminic acid acidolysis by the carboxylic acid, with formation of the phenylamide. Unsubstituted sulfaminic acid and alkylsulfaminic acids do not react, under similar conditions, with carboxylic acids. Thus the proposed amidation mechanism fully explains all of the known facts. But theory should not only explain, it should also predict. Thus, the second stage of the reaction is found to be aminolysis of acylsulfoaminic acid according to the scheme:



$$\begin{matrix} RCO-NHSO_2OH \\ + \\ H_2N-H \end{matrix} \longrightarrow RCONH_2 + NH_2SO_2OH.$$

Therefore, the first deduction is: If the amidation reaction is carried out with an unsubstituted sulfamide in the presence of an "auxiliary" amine, then a substituted amine should result, for example:

$$RCOOH + NH_2SO_2NH_2 \rightarrow RCONHSO_2ONH_4;$$

$$RCONHSO_2ONH_4 + C_6H_5NH_2 \rightarrow RCONHC_6H_5 + NH_2SO_2ONH_4.$$

This deduction was confirmed in the case of sulfamide-p-nitrobenzoic acid-aniline. Calculated on the basis of p-nitrobenzoic acid which entered into reaction, there was obtained: phenylamide, 58% of theoretical, unsubstituted amide – about 36% of the theoretical.

Production of the phenylamide may also be explained by the fact that the aniline reacts with sulfamide to give phenylsulfamide and diphenylsulfamide, which then phenylamidates the acid:

$$NH_2SO_2NH_2 \xrightarrow{C_6H_5NH_2} C_6H_5NHSO_2NH_2 \xrightarrow{C_6H_5NH_2} C_6H_5NHSO_2NHC_6H_5;$$

$$2RCOOH + C_6H_5NHSO_2NHC_6H_5 \rightarrow 2RCONHC_6H_5 + H_2SO_4.$$

Experiment (see experimental portion [7]) has shown that the reaction indeed does also proceed in this direction, but even under conditions considerably more favorable for sulfamide phenylation, only 14% diphenylamide is formed and can only produce at the utmost about 21% of phenylamide. However, in actuality this quantity is much smaller, since the rate of reaction of acid with sulfamide is much higher than the sulfamide reaction rate with aniline. Hence if follows that the main bulk of phenylamide is formed at the expense of phenylaminolysis of acylsulfaminic acid.

Moreover, the phenylamide formation can be explained by a reamidation of unsubstituted amide during reaction with aniline. Specially arranged experiments indicated that under the specified conditions reaction does not proceed significantly.

Second deduction: During reaction with prepared acylsulfaminic acids of ammonia (or of amines) the amides (or substituted amides) of the carboxylic acids and of sulfaminic acid should result:

$$RCONHSO_2OH + C_6H_5NH_2 \rightarrow RCONHC_6H_5 + NH_2SO_2OH.$$

This hypothesis was experimentally verified by heating benzamide and betainopyridinium-sulfaminic acid mixture [8] to obtain the pyridine salt of benzoyl sulfaminic acid. The reaction mixture (without isolation of the benzoylsulfaminic acid) was heated with aniline. About 70% of the theoretical quantity of benzanilide (calculating on the basis of benzamide entering into reaction) was isolated. It follows that the second deduction is also experimentally confirmed.

Thus the proposed theory for the amidation mechanism of carboxylic acids by sulfamides not only confirmed all known experimental data, but also gave an opportunity for predicting two new reactions; therefore there are grounds to believe that the proposed mechanism is correct.

EXPERIMENTAL

Interaction of Tetrasubstituted Sulfamides with Carboxylic Acids. Acetic and benzoic acids, symmetrical dimethyldiphenylsulfamide [7], diethyldiphenylsulfamide and tetramethylsulfamide [9] were selected as the experimental compounds. Six experiments in all were carried out, of which one is described in detail, namely the interaction of benzoic acid and dimethyldiphenylsulfamide.

0.01 mole of dimethyldiphenylsulfamide (2.76 g), 0.01 mole of benzoic acid (1.22 g) and 5.0 ml of dry pyridine mixture were heated for 4 hours with a reflux condenser on an oil bath at 116°. The reaction mixture remained transparent, and the yellowing was hardly noticeable. The pyridine was distilled off in vacuo, the crystalline residue was treated with 15 ml of 1.0 N caustic soda solution, and then with 100 and with 50 ml of ether. The ether solution was dried with Na_2SO_4, and the ether was distilled off. The crystalline residue was dried over H_2SO_4 in vacuo of 0.5 mm for 24 hours and represented pure dimethyldiphenylsulfamide. Yield was 2.74 g (99.2% of the quantity taken), m.p. 95.5-97.0°, a sample mixed with known dimethyldiphenylsulfamide melted at 96.0-97.0° (uncorrected).

The alkaline solution was acidified with 10.0 ml of 2.0 N hydrochloric acid, and the benzoic acid was extracted with ether. The ether solution was dried with Na_2SO_4, the ether distilled off, and the residue dried over H_2SO_4 in vacuo of 0.5 mm. The yield of benzoic acid was 1.20 g (98.2% of the quantity taken), m.p. 119-120°, a sample mixed with known benzoic acid melting at 119.5-121°.

The remaining five experiments were carried out under the same conditions. In all cases the tetrasubsituted sulfamides were recovered in quantities amounting to 99.1-99.4% of the original, benzoic acid in quantities of 97.8-98.5% of original. Acetic acid was not separated.

Reaction of Dimethylphenylsulfamide with Benzoic Acid. 0.01 mole of dimethylphenylsulfamide (2.0 g), 0.01 mole of benzoic acid (1.22 g) and 5.0 ml of dry pyridine were heated for 3 hours on an oil bath at 115°. The pyridine was distilled off in vacuo and the residue was treated with 150.0 ml of ether and 10 ml of 2.0 N HCl. After vigorous shaking, the ether solution was separated, washed three times with 1.0 ml portions of water, then with 15 ml of 1.0 N caustic soda solution, dried with Na_2SO_4 and evaporated to dryness. The residue consisted of 1.42 g of benzanilide and benzdimethylamide mixture. For separation, the mixture of amides was treated with 30 ml of petroleum ether (b.p. 85-95°) in which the benzdimethylamide is very readily soluble, and the undissolved benzanilide was filtered off with suction and washed 3 times with 1.0 ml portions of petroleum ether. Yield 0.65 g (33.0% of theoretical). After recrystallization from alcohol, large lustrous flakes resulted, m.p. 161-162° (uncorrected), which did not give depression with authentic benzanilide.

The filtrate was treated with 0.1 g of activated charcoal and evaporated in vacuo. The resulting colorless oil, upon addition of benzdimethylamide seeder crystallized immediately to a completely dry, crystalline mass. Yield was 0.75 g (50.2% of the theoretical), m.p. 39-41° (uncorrected), which did not give depression with an authentic sample of benzdimethylamide.

Reaction of Dimethylphenylsulfamide with p-Nitrobenzoic Acid. 0.01 mole of dimethylphenylsulfamide (2.0 g), 0.01 mole of p-nitrobenzoic acid (1.76 g) and 5.0 ml of pyridine mixture were heated for 3 hours on an oil bath at 115°. After distilling off the pyridine in vacuo, 10.0 ml of 1.0 N caustic soda solution and 40.0 ml of water were added to the residue. After 20 minutes, the fine, crystalline precipitate was filtered off with suction and washed 4 times with 5.0 ml portions of water. The precipitate (0.99 g) consisted principally of p-nitrobenzoic acid phenylamide, but also contained a certain amount of dimethylamide. A considerable quantity of dimethylamide was present in the aqueous filtrate which was extracted three times with 5 ml portions of ether. The ether solution was dried with Na_2SO_4 and the ether distilled off. The residue was dried in vacuo over sulfuric acid. After drying, 0.93 g of crude dimethylamide of p-nitrobenzoic acid resulted.

The phenylamide and the dimethylamide were separated by the use of petroleum ether (b.p. 85-95°).

The mixture of amides (0.99 g) was boiled with 75 ml of petroleum ether, the undissolved phenylamide removed by suction at the boiling point and washed 3 times with 5 ml portions of boiling petroleum ether. 0.70 g (28.9% theoretical) of p-nitrobenzoic acid phenylamide resulted, in the form of a dirty-gray, fine crystalline powder with m.p. 208-210°. After recrystallization from 15 ml of butanol, the phenylamide resulted in the form of almost colorless, large, flat needles with m.p. 210-211° (uncorrected), which did not give a depression with known p-nitrobenzanilide.

To remove the phenylamide from the petroleum ether solution, 0.2 g of activated charcoal was added to the solution, cooled to 75°, and filtered at the same temperature. After cooling, the p-nitrobenzoic acid crystals crystallized out in the form of thin, colorless needles.

The crude dimethylamide (0.98 g) was also crystallized from 75 ml of boiling petroleum ether with addition of 0.2 g of activated charcoal and filtraion at 75°. The total yield of dimethylamide was 1.20 g, i.e., 61.9% of the theoretical quantity, m.p. 93-95° (uncorrected), which did not give depression with authentic p-nitrobenzoic acid dimethylamide.

Synthesis of the Phenylsulfaminic Acid Ammonium Salt. 0.2 mole of freshly distilled aniline (18.6 g) was heated on a wire screen in a conical flask of 50 ml volume, and to the aniline was added in small portions, with very vigorous hand shaking, over a period of 10-15 minutes, finely-ground, dry sulfaminic acid in the amount of 0.1 mole (9.7 g). Care was taken that the sulfaminic acid did not adhere to the bottom and to the walls of the flask. During the addition of sulfaminic acid, the temperature of the reaction mixture, as measured by a thermometer immersed in it, was maintained in the range 160-170°. After all of the sulfaminic acid had been added, the reaction mixture was boiled gently for 5 minutes. After cooling, the reaction mixture crystallized to a light pink, solid mass. To remove aniline, the mixture was washed 3 times with 30 ml portions of dry benzene, each time mixing the whole mass thoroughly. The viscous mass after a third washing, became crumbly and hard. After 15 minutes the product was filtered off with suction and washed on the filter, mixing thoroughly each time, with 15 ml portions of benzene, and 3 times with15ml portions of absolute ether. Following this the product was dried in vacuo over sulfuric acid. The crude ammonium salt of phenylsulfaminic acid represented a fine crystalline, almost colorless, powder. Yield was 17.0 g (89.4% of the theoretical).

Reaction of Phenylsulfaminic Acid Ammonium Salt with p-Nitrobenzoic Acid. 0.01 mole of p-nitrobenzoic acid (1.67 g) and 5.0 ml of dry pyridine were heated to the dissolution of the acid, and to the solution was immediately added, with vigorous hand shaking, 0.01 mole crude ammonium salt of phenylsulfaminic acid (1.9 g). The salt at first dissolved immediately, and then rapidly precipitated considerable sediment, and the mixture became yellow. The reaction mixture was heated for 2 hours on a reflux, in an oil bath at 115°. During that time the sediment almost completely went into solution, but the liquid remained turbid. The pyridine was distilled in vacuo, and to the residue was added 25.0 ml of 1.0 N caustic soda solution, the finely, crystalline, almost colorless precipitate filtered off with suction and washed 4 times with 5 ml portions of water. Yield of p-nitrobenzoic acid phenylamide was 0.75 g (30.9% of theoretical), m.p. 206-208°; after recrystallization from 15 ml of butanol – large, flat needles, m.p. 210-211°; did not give depression with known p-nitrobenzanilide.

Interaction of Diphenylsulfamide with Two Molecules of p-Nitrobenzoic Acid. 0.01 mole of p-nitrobenzoic acid (1.67 g), 0.005 mole of diphenylsulfamide (1.24 g) and 5.0 ml of dry pyridine mixture were heated for 6 hours on an oil bath at 115°. The pyridine was distilled off in vacuo, and to the residue was added 25.0 ml of caustic soda solution. After 15 minutes the crystalline precipitate was filtered off with suction and washed 4 times with 5.0 ml portions of water. The crude p-nitrobenzanilide – fine gray crystals with m.p. 208-210° – did not give a depression with known nitrobenzanilide. Yield 1.78 g, i.e., 147.2% of theory, calculating on the basis of the general scheme of amidation, or 73.6% of theory, considering that the phenylsulfaminic acid is also an amidating agent. After recrystallization from 25.0 ml of butanol, large, flat needles resulted with m.p. 210-211°.

Interaction of Sulfamide, p-Nitrobenzoic Acid and Aniline. 0.01 mole of sulfamide (0.96 g), 0.02 mole of aniline (1.86 g). 0.01 mole of p-nitrobenzoic acid (1.67 g) and 5.0 ml of dry pyridine mixture were heated for 3 hours on an oil bath at 115°. The pyridine was distilled off in vacuo, and to the residue was added 25 ml of 2.0 N hydrochloric acid. The precipitated, finely crystalline, almost colorless crystals were washed 4 times with 5.0 ml portions of water, and then treated on the funnel with 10.0 ml of 1.0 N caustic soda solution, and again washed 4 times with 5 ml portions of water. From the alkaline filtrate upon acidification 0.12 g separated, i.e., 7.2% on the basis of p-nitrobenzoic acid used. M.p. 234-236° did not give a depression with known p-nitrobenzoic acid. 1.86 g of product, insoluble in alkali, was obtained, i.e., 112% of theory on the basis of amide; on the basis of phenylamide – 76.9% of theory. The product melted slowly in the range 170-191°, and represented a mixture of amide and phenylamide. To separate, all of the mixture (1.86 g) was boiled with 100 ml of water; the undissolved portion (phenylamide) filtered off from the boiling solution with suction and washed twice with 5 ml portions of boiling water. 1.2 g of crude p-nitrobenzanilide with m.p. 199-205° resulted; melting point of the mixed sample with p-nitrobenzamide was 160-190°. After recrystallization from 25 ml of butanol large flat needles resulted, with m.p. 210-211°.

The aqueous filtrate from p-nitrobenzanilide was heated to boiling, cooled to 75°, and at the same time a small quantity of very fine crystals separated out, which were filtered off. After cooling, very nice long needles of p-nitrobenzamide separated out. Yield was 0.36 g, m.p. 195-197°; mixed sample with known p-nitrobenzamide melted at 196-197°. Thus, the loss upon separation and crystallization constituted 0.3 g. Insofar as the unsubstituted amide is more readily soluble, this accounts for the loss of 0.2 g, and for the phenylamide 0.1 g. Accordingly, the total yield of phenylamide was about 1.3 g, i.e. about 50% of theory, calculating on the basis of p-nitrobenzoic acid entered into reaction, and the yield of unsubstituted amide about 0.56 g, about 36% theoretical, calculating also on the basis of p-nitrobenzoic acid, entered into reaction.

Phenylation of Sulfamide by Aniline in Pyridine Solution. 0.01 mole of sulfamide (0.96 g), 0.02 mole of aniline (1.86 g) and 5.0 ml of dry pyridine mixture were heated for 6 hours on an oil bath at 115°. The pyridine was then distilled off in vacuo, and to the residue was added 15.0 ml of 2.0 N hydrochloric acid, and the liquid extracted 3 times with 50 ml portions of ether. The ether extracts were washed three times with 3 ml portions of water and then extracted by 5 ml of 1.0 N caustic soda solution. 2.0 ml of 10.0 N sulfuric acid was added to the alkaline extract, at which time an oil separated which rapidly crystallized. The product was filtered off with suction, washed with water and dried in air. The yield of diphenylsulfamide was 0.35 g (14.1% of theory), m.p. 108-111°, and did not give depression with known sample of diphenylsulfamide. The aqueous mother liquor contained monophenylsulfamide. A better yield resulted when sulfamide was heated with a very large excess of aniline (10.0 ml of aniline for 0.01 mole of sulfamide) at 115°. According to A. Paquin [7], diphenylsulfamide results in 84% yield upon heating equimolecular quantities of aniline and sulfamide at 120-155° for 5.5 hours. This is inaccurate, since under such conditions only 10-15% of diphenylsulfanide results.

Interaction of p-Nitrobenzamide and Aniline in Pyridine Solution. 0.01 mole of p-nitrobenzamide (1.66 g) 0.02 mole of aniline (1.86 g) and 5.0 ml of dry pyridine mixture were heated for 3 hours on an oil bath at 115°. The pyridine was distilled off in vacuo, the residue was treated with 25.0 ml of 2.0 N hydrochloric acid and after 10 minutes the undissolved crystalline precipitate was filtered off with suction and washed 4 times with 5 ml portions of water. 1.61 g of p-nitrobenzamide resulted, with m.p. 195-197°, which did not give depression with known p-nitrobenzamide.

Benzoylsulfaminic Acid Interaction with Aniline. 0.01 mole of betainopyridinium-sulfaminic acid (1.59 g) and 0.01 mole of benzamide (1.21. g) mixture was heated on an oil bath to melting at 160°, plus an additional minute [8]. To the resulting melt was then added 0.02 mole of aniline (1.86 g) and the mixture was heated on an oil bath at 120° for 2 hours. After cooling, 20 ml of water was added, , the fine crystalline precipitate was filtered off with suction and then washed twice with 5 ml portions of water, once with 5 ml of 1.0 N soda solution, 4 times (in 5 ml portions) with water and 3 times with 1 ml portions of alcohol. The yield of benzanilide was 0.35 g (70.4% of theory, based upon benzamide entered into reaction), m.p. 160-161°, and did not give depression with known benzanilide. After recrystallizing from 5 ml of alcohol, the benzanilide resulted in the form of large lustrous flakes, with m.p. 161-162°.

The aqueous filtrate from the benzanilide was acidified with hydrochloric acid to an acid reaction with Congo, and extracted 5 times (in 50 ml portions) with ether. The ether extracts were dried with Na_2SO_4, the ether distilled off to a volume of about 5 ml and the large transparent prisms which separated out were washed 3 times with 1 ml portions of ether. Yield of benzamide was 0.75 g, m.p. 126-127°, and did not give depression with known benzamide. From the ethereal mother liquor an additional 0.16 g of benzamide, with m.p. 122-126°, was isolated. Total yield of benzamide was 0.91 g (75% of the initial quantity).

SUMMARY

A theory for the amidation mechanism of carboxylic acids by sulfuric acid amides has been proposed and experimentally confirmed.

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* See Consultants Bureau translation, p. a-675.

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THE ABNORMAL REDUCTION OF β-SUBSTITUTED PROPIONITRILES ACCORDING TO VYSHNEGRADSKY

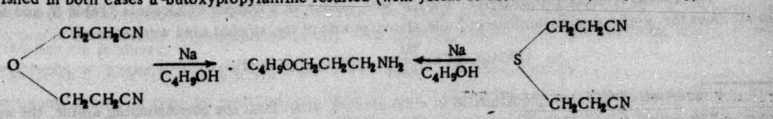
A. N. Kost and V. G. Yashunsky

The method of reducing organic compounds by the use of metallic sodium in an alcoholic medium was proposed for the first time in 1879 by a student and co-worker of A. N. Butlerov – a Russian scientist by the name of A. N. Vyshnegradsky [1]. While studying alkaloid structures, Vyshnegradsky obtained ethylpiperidine from ethylpyridine by this method. His untimely death in 1880 disrupted these brilliant experiments. In 1884, a German scientist, Ladenburg, applied the Vyshnegradsky method to the reduction of other pyridine homologs, and having somewhat modified the method of synthesizing bases, attributed this discovery to himself [2]. The Vyshnegradsky method was extended further to include various classes of organic compounds. It was found that not only could heterocyclic bases of the pyridine or quinoline type be reduced, but also nitriles, oximes, amides, ketones, lactones, esters, halogen derivatives, certain aromatic compounds, and others. At the present time the Vyshnegradsky method is widely used by chemists for the investigation of organic chemical structure, or for preparatory purposes. The qualitative determination of halogens according to Stepanov is based upon this method. A. N. Vyshnegradsky's priority is unquestionable; however, this method is frequently attributed to Ladenburg, or even to Buvo, while the latter only applied the Vyshnegradsky method to the reduction of esters [3].

In the preceding articles [4.5] several examples of the application of Vyshnegradsky's method to the synthesis of certain diamines from aminonitriles was described. At the same time, the authors pointed out some instances of abnormal reactions, namely that small additions of potassium to sodium markedly lower amine yields, but when the potassium content reaches 2%, the yield again increases [6].

Reduction of nitriles, according to Vyshnegradsky, proceeds differently, depending upon the initial nitrile structure. It is known that upon reduction by sodium in alcohol, some nitriles become split at the CN groups with formation of the corresponding hydrocarbon + sodium cyanide. Thus Walter and McElvain [7], by reduction of benzonitrile, obtained benzylamine, but only in 7% yield, and from phenylacetonitrile they obtained toluene (in 90% yield). Likewise, during the reduction of diphenylacetonitrile, there was obtained, along with the corresponding amine, a considerable quantity of diphenylmethane [8]. During the reduction of α-aminoisobutyronitrile, isopropylamine was isolated [9], and the nitrile of α-phenylcinnamic acid converted almost completely into α,β-diphenylethane [10].

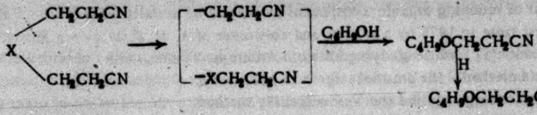
The authors have indicated earlier that an eight-membered piperazine analog results from dicyandiethylamine, namely, 1,5-diazacyclooctane [5]. It was of interest to reduce other dinitriles of the same type under the same conditions: $NCCH_2CH_2XCH_2CH_2CN$, where X = CH_2, O, S. During reduction of pimilonitrile (X = CH_2), the authors did not succeed in isolating the cyclic compound, and instead heptamethylenediamine resulted in 72% yield, which corresponded to the data of Brown [11]. During reduction of β,β'-dicyandiethylester (X=0) by sodium in butyl alcohol, the authors did not obtain a fraction corresponding to the linear diamine, but rather a considerable quantity of lower boiling substance resulted, which, from the constants and by analysis, was erroneously taken by the authors to be the cyclic amine, i.e., 1-oxy-5-azacyclooctane [12]. However, when the authors reduced β,β'-dicyandiethylsulfide (X=S) under the same conditions, it was then found unexpectedly that the reaction product was exactly identical with the one resulting from reduction of its oxide analog. By an investigation of the structure through its spectrum and by alternate synthesis, it was established in both cases α-butoxypropylamine resulted (with yields of 58.6 and 21.9% respectively).



Seeger [13] observed a similar phenomenon when heating esters and nitriles of β-alkoxypropionic and butyric acids with alcohols in the presence of metallic sodium. He found that there occurs an exchange of the alkoxy group for the radical of the alcohol introduced into the reaction. Thus from a 4-hour heating of 1 mole of β-methoxyisobutyronitrile, 5 moles of allyl alcohol and 5 g of metallic sodium mixture, β-allylhydroxyisobutyronitrile was isolated.

A comparatively easy cleavage of the dicyandiethyl ester was observed earlier during catalytic hydrogenation. Thus, Whitmore and his co-workers [14] found that upon hydrogenating this dinitrile over nickel catalyst, γ,γ-diaminodipropyl ester resulted; later, however, it was found that in reality a mixture of this diamine with propanolamine is formed [15].

The authors' experiments have shown that upon reduction with sodium in alcohol of the corresponding sulfide of the dicyandiethyl ester, cleavage occurs at the C-O or at the C-S bonds. The nitrile group is reduced only after addition of the alcohol. The linear amine, even upon thorough search, was not found by the authors.



For an explanation of the transformation mechanism which occurs, the authors have used simpler forms, namely the β-alkoxypropionitriles. It was found that if a propionitrile was used, with the same β-alkoxy group as for the alcohol in which the reaction was carried out, that a normal reaction product will result in the Vyshnegradsky reaction, i.e., the amine corresponding to the nitrile introduced, for example, β-ethoxypropionitrile in ethyl alcohol gives γ-ethoxypropylamine.

In the case where alkoxynitrile and alcohol radicals did not coincide, then in the final outcome, β-alkoxypropylamine with the alkoxy group of the alcohol was formed in the reduction.

Thus, upon reducing β-methoxypropionitrile and β-(β-hydroxyethoxy)-propionitrile in n-butyl alcohol, the authors isolated in both cases γ-butoxypropylamine. Upon reducing β-phenoxypropionitrile in ethyl alcohol, the authors obtained γ-ethoxypropylamine in 55% yield, while at the same time in almost all cases the normal reaction products were not found (Table 1).

TABLE 1

Reduction of β-Alkoxypropionitriles

Alcohol in which reduction was carried out.	initial alkoxynitrile $ROCH_2CH_2CN$ R =	resulting amine $ROCH_2CH_2NH_2$ R =	boiling point		picrate melting point	yield (%)
			(°C)	(mm)		
ethyl	C_2H_5	C_2H_5*	54–55	39	–	48.2
ethyl	C_6H_5	C_2H_5	59–60	48	–	55.5
isopropyl	iso-C_3H_7	iso-C_3H_7	74–75	68	–	21.5
n-butyl	n-C_4H_9	n-C_4H_9	80–81	24	96°	50.5
n-butyl	CH_3	n-C_4H_9	69–70	18	96°	25.8
n-butyl	$HOCH_2CH_2$	n-C_4H_9	57–58	8	95.5°	29.4
isoamyl	iso-C_5H_{11}	iso-C_5H_{11}**	82–83	20	104°	51.6

An even more simple example seems to be that of ethylenecyanhydrin (i.e., β-hydroxypropionitrile), while at the same time there are data in the literature only for its catalytic hydrogenation [16].

The authors reduced β-hydroxypropionitrile with sodium in a number of alcohols (Table 2) and found that in all cases the γ-alkoxypropylamines with the alkoxy groups of the alcohol used were formed:

$$HOCH_2CH_2CN \xrightarrow[ROH]{Na} ROCH_2CH_2CH_2NH_2.$$

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* During reduction of β-ethoxypropionitrile in ethyl alcohol, apart from the corresponding amine, the authors isolated a base with b.p. 116-117° at 18 mm, to which can be attributed, on the basis of constants and of analysis, the diamine structure resulting from reduction of cyanethylated γ-ethoxypropylamine:

(see next page for continued footnotes)

In every case, the authors failed to isolate γ-propanolamine and other bases from the reaction products.

The explanation for the transformations during reduction by sodium in alcohols of β-alkoxypropionitriles can be given in two ways: either by direct realkylation of alkoxynitriles, or by intermediate formation of acrylonitrile, when this adds to the alcohol which has been used as the medium for the reaction, thus giving the corresponding alkoxynitrile. Subsequent reduction of the β-alkoxynitriles thus formed leads to the γ-alkoxyamines.

TABLE 2

β-Hydroxypropionitrile Reduction

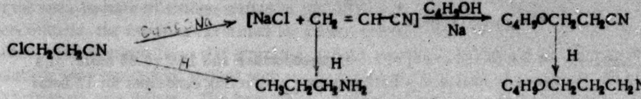
alcohol in which reduction was carried out	resulting amine $ROCH_2CH_2CH_2NH_2$ R =	boiling point of amine (°C)	boiling point of amine (mm)	yield (%)
ethyl	C_2H_5	58−59	45	21.0
isopropyl	iso-C_3H_7	78−79	86	20.0
n-butyl	n-C_4H_9	68.5−69.5	17	20.0
isobutyl	iso-C_4H_9***	65−66	20	24.4
isoamyl	iso-C_5H_{11}	66−67	12	36.4

$$\text{I. } ROCH_2CH_2CN + R'OH \xrightarrow{-ROH} R'OCH_2CH_2CN \xrightarrow{H} R'OCH_2CH_2CH_2NH_2;$$

$$\text{II. } ROCH_2CH_2CN \rightarrow ROH + CH_2{=}CH{-}CN;$$
$$CH_2{=}CH{-}CN + R'OH \rightarrow R'OCH_2CH_2CN;$$

$$R'OCH_2CH_2CN \xrightarrow{H} R'OCH_2CH_2CH_2NH_2.$$

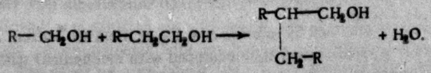
The second reaction course seemed more probable to the authors. This also confirms the reduction experiments of β-chlorpropionitrile in butyl alcohol. The authors isolated γ-butoxypropylamine in 68% yield, and some quantity of propylamine, i.e., the reaction course was as follows:



To verify these assumptions, the authors reduced acrylonitrile with sodium in a number of alcohols. As was to be expected, the principal reduction products were found to be γ-alkoxypropylamine, corresponding to the alcohols used.

From these experimental results it was found possible to make a deduction concerning the transformation mechanism which occurs in the abnormal Vyshnegradsky reaction, as discovered by the authors. Under the authors' conditions, β-hydroxypropionitrile is partially dehydrogenated, and the resulting acrylonitrile reacts further according to the scheme given. Low yields of alkoxypropylamines can be explained by the appearance of water in the reaction medium, and as is known, the reduction of nitriles or of esters by sodium in non-absolute alcohol gives poor yields of final products [17]. However, the authors failed to find at any time the presence of the acid which might be formed by hydrolysis of the nitrile.

Moreover, as has been shown by Guerbet [17a] and Terentyev[18], alcohols in the presence of alcoholates may enter into condensations of the type:



$$R{-}CH_2OH + R{-}CH_2CH_2OH \longrightarrow \begin{array}{l} R{-}CH{-}CH_2OH \\ \;\;\;\; | \\ \;\;\; CH_2{-}R \end{array} + H_2O.$$

Under the authors conditions, this reaction could take place all the more readily, since the hydrogen atom of β-hydroxypropionitrile, by virtue of its being in the α-position to the nitrile group, is sufficiently mobile. The products of such condensation can undergo reduction, and isolation of the resulting bases is quite difficult. Thus, with a certain degree of probability, the low yields of amines upon reduction of β-hydroxypropionitrile can be explained. Reduction of β-alkoxypropionitriles evidently proceeds according to scheme II given above. At the same time, a partial reduction of acrylonitrile to propylamine occurs. The resulting amine can be cyanethylated, while, on reduction, alkoxydiamines are produced.

$$C_2H_5OCH_2CH_2CH_2NH_2 + CH_2{=}CH{-}CN \rightarrow [C_2H_5O(CH_2)_3NHCH_2CH_2CN] \xrightarrow{H} C_2H_5O(CH_2)_3NH_2$$

In other experiments of similar type, no fractions were isolated, due apparently to their high boiling points.

** γ-Isoamylpropylamine has been synthesized by the authors for the first time: n_D^{20} 1.4312; d_4^{20} 0.8517; MR_D 44.17; $C_8H_{19}ON$. Calculated MR_D 44.21

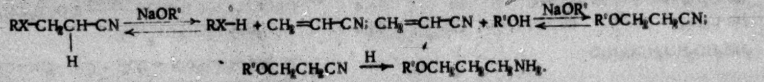
*** γ-Isobutoxypropylamine has been synthesized for the first time: n_D^{20} 1.4246; d_4^{20} 0.8448; MR_D 39.63; $C_7H_{17}ON$. Calculated MR_D 39.59. Picrate – m.p. 100°.

In the case of the dicyandiethyl ester, the cleavage products are found to be acrylonitrile and ethylenecyanhydrin, while the latter may become partially dehydrogenated to acrylonitrile:

$$NCCH_2CH_2OCH_2CH_2CN \longrightarrow NCCH_2CH_2OH + CH_2{=}CH{-}CN;\ HOCH_2CH_2CN \longrightarrow CH_2{=}CH{-}CN + H_2O.$$

Reaction of the sulfide analog proceeds in a similar fashion.

Thus the authors have observed realkylation of β-halo, β-thio, β-hydroxy and β-alkoxy-propionitriles under the conditions of the Vyshnegradsky reaction. This phenomenon can be explained on the basis of mobility of the hydrogen atom which is in the α-position to the nitrile group, which facilitates ready splitting of the molecule, especially in alkaline medium. This reaction is reversible, but the acrylonitrile resulting from such a cleavage enters into reaction almost exclusively with the alcohol that has been used in the capacity of a medium for reduction, since this alcohol is present in large excess (nitrile: alcohol = 1:45). Thus the equilibrium is greatly shifted toward the right. Reduction of the nitrile group removes the nitrile from reaction, which shifts the equilibrium even more:



$$RX{-}CH_2\underset{\textstyle H}{\underset{|}{C}}H{-}CN \overset{NaOR'}{\rightleftarrows} RX{-}H + CH_2{=}CH{-}CN;\ CH_2{=}CH{-}CN + R'OH \overset{NaOR'}{\rightleftarrows} R'OCH_2CH_2CN;$$

$$R'OCH_2CH_2CN \xrightarrow{H} R'OCH_2CH_2CH_2NH_2.$$

If the β-alkoxy- or the β-thio-nitriles do not have α-hydrogens, then such nitriles should be transformed during the Vyshnegradsky reaction. In actuality, Cass [19] obtained a good yield of corresponding diamine during reduction of the nitrile from thiodipivalic acid.

It is interesting to note that during reduction of β-aminopropionitriles under the Vyshnegradsky conditions, there was not observed in noticeable quantities formation of any alkoxypropylamines. Apparently, the β-aminopropionitriles are stable in the presence of alkaline reagents.

EXPERIMENTAL

Synthesis of Pimelonitrile [20]. 38.2 g (0.165 mole) of 1,5-dibromopentane and 17.2 (0.35 mole) of a water-alcoholic solution of sodium cyanide were heated in a flask equipped with reflux condenser for 10 hours on a water bath. The alcohol was then distilled off, and the residue was redistilled with steam to remove unreacted dibromide. The remaining brown oil was extracted with ether, the ether solution washed with dilute alkali and dried over anhydrous calcium chloride, after which the ether was distilled off and the nitrile was fractionated at low pressure. 13.7 g (68% of theory) of the pimelonitrile resulted, b.p. 159-160° at 8 mm.

Literature data: b.p. 171-172° at 12 mm [20].

Synthesis of β-Alkoxypropionitriles. These were prepared by the authors according to the method of MacGregor [21], by the interaction of acrylonitrile with alcohols in the presence of sodium alcoholate.

β-Methoxypropionitrile. 0.9 g of metallic sodium was added to 24 g (0.4 mole) of methyl alcohol over a period of 30 minutes, and with external cooling and stirring, there was added dropwise 21.2 g (0.4 mole) of freshly-distilled acrylonitrile. The mixture was then heated on a water bath with stirring for another hour, and was then neutralized with 20% sulfuric acid. The alcoholic layer was separated and dried with anhydrous sodium sulfate. 26.5 g (78% of theory) of β-methoxypropionitrile resulted with b.p. of 163-164°. β-Ethoxypropionitrile and β-isopropoxypropionitrile were obtained by the same procedure, with yields, respectively, of 76.8 and 71%. The nitrile constants corresponded with the literature data [22].

β-Isoamylhydroxypropionitrile. The alcoholate obtained by solution of 0.1 g of metallic sodium in 52.8 g (0.6 mole) of absolute isoamyl alcohol was placed in a three-necked flask equipped with mechanical stirrer, dropping funnel and reflux condenser. 31.8 g (0.6 mole) of acrylonitrile was added dropwise to the alcoholate (at 80° with stirring.). The mixture was then heated on a water bath, stirred for 1 hour, and then neutralized with dilute sulfuric acid. The alcoholic layer was separated, dried with anhydrous sodium sulfate and redistilled. 64.2 g (75.9% theoretical) of β-isoamylhydroxypropionitrile resulted; b.p. 109-110° at 22 mm.

Literature data: b.p. 99° at 13 mm [23].

β-Butoxypropionitrile was obtained in the same manner with 78.5% yield.

β-Phenoxypropionitrile [24]. 121 g (1.28 moles) of phenol and 1.5 g of metallic sodium were placed in a three-necked flask equipped with mechanical stirrer, reflux condenser and dropping funnel. Then, over a period of one hour, and at 130-135°, 67.8 g (1.28 moles) of acrylonitrile was added, and the mixture stirred for another 5 hours at the same temperature. After cooling, the flask contents were treated with 10% caustic soda solution and with ether. The ether layer was separated, washed repeatedly with the alkali solution, then with dilute hydrochloric acid and finally water. A crystalline mass remained after distilling off the ether. After recrystallization from cyclohexane —white flakes with m.p. 62°. 98.2 g of pure β-phenoxypropionitrile resulted (52% of theory).

Literature data: m.p. 61-62° [24].

β-(β'-Hydroxyethoxy)propionitrile. 39.8 g (0.75 mole) of acrylonitrile was added dropwise over a period of 2 hours to a cooled mixture of 46.5 g (0.75 mole) of ethylene glycol and 1.8 g of 25% aqueous caustic soda solution. The resulting yellow viscous mass was neutralized with dilute sulfuric acid. The organic layer was separated, dried with sodium sulfate, and fractionally distilled. Unreacted acrylonitrile was distilled off at atmospheric pressure, and the distillation then continued at decreased pressure. Three fractions were collected: I) up to 100° at 5 mm (mainly ethylene glycol); II) b.p. 132-135° at 5 mm —44.6 g; III) b.p. 160-171° at 3 mm —25 g.

The second fraction —monocyanethylated ethyleneglycol —was distilled repeatedly; b.p. 111-112° at 1.5 mm. Yield 47.8 g, calculated for acrylonitrile; n_D^{20} 1.4443; d_4^{20} 1.0793; MR_D 28.35; calculated 28.29.

The third fraction corresponded to dicyanethylated ethylene glycol, b.p. 186° at 9 mm [25]; 158° at 2 mm [26].

β,β'-Dicyandiethyl Ester. This ester was obtained by Bruson's method [27], by the interaction of acrylonitrile with ethylenecyanhydrin in the presence of alkali. B.p. 164-165° at 8 mm, which corresponded to the literature data [27].

β,β'-Dicyandiethylsulfide. The authors obtained this ester by reacting acrylonitrile with an aqueous solution of sodium sulfide [28]. 79.5 g (1.5 moles) of acrylonitrile was added to a solution of 180 g (0.75 mole) of the nona-hydrate of sodium sulfide in 100 ml of water, with stirring and cooling to 10°. After addition of the acrylonitrile, the mixture was stirred for 4 hours at room temperature, following which 200 ml of benzene was added. The benzene layer was separated, and the aqueous layer washed several times with benzene. The benzene solutions were combined, washed with small portions of dilute hydrochloric acid and water, and then dried over anhydrous sodium sulfate. The benzene was distilled off and the residue redistilled in vacuo. 89 g of β,β'-dicyandiethylsulfide resulted (i.e. 85% of theory). The viscous, colorless liquid crystallized upon standing. B.p. 178-179° at 3 mm.

Literature data: b.p. 191-194° at 7 mm [29].

β-Chloropropionitrile. Prepared through the action of dry hydrogen chloride upon acrylonitrile with cooling. B.p. 59-60° at 8 mm, which corresponded to the literature data [30].

Reduction of Pimelonitrile

A heated solution of 8.9 g (0.073 mole) of pimelonitrile in 330 ml of absolute n-butyl alcohol was added to 22 g of metallic sodium placed in a liter round-bottomed flask, equipped with a two-horned adapter and a heavy-duty copper reflux condenser. An oil bath preheated to 145° was immediately placed under the flask. This temperature was maintained until the sodium had completely dissolved; after that the mixture was cooled, and the resulting alcoholate decomposed with water. The alcohol and the base were distilled off over a period of several hours with superheated steam into a receiver containing dilute hydrochloric acid. From this solution the butyl alcohol was distilled out with steam, and the residue was condensed on a water bath. The crude hydrochloride was decomposed with powdered sodium hydroxide and the resulting base was repeatedly extracted with ether. The ether solution (about 300 ml) was dried with anhydrous caustic potash, and was fractionated after distilling off the ether. The first fraction —up to 91° at 7 mm negligible. The second fraction —heptamethylenediamine, with b.p. 91-92° at 7 mm —was collected in the amount of 6.41 g, which constituted 71.5% of theory. Upon standing, the diamine crystallized to form low-melting crystals. Benzoyl derivative —colorless needles from alcohol; m.p. 123°.

Literature data: b.p. 223-225°; benzoyl derivative —m.p. 123.5° [31].

Reduction of β,β'-Dicyandiethyl Ester

Reduction was carried out in like manner. 12.4 g (0.1 mole) of dicyandiethyl ester, 30 g of sodium and 430 ml of absolute n-butyl alcohol were taken. After reduction, the mixture was decomposed with water (100 ml).

The alcoholic layer was then separated, and the aqueous-alkaline residue washed with small portions of butyl alcohol. The combined alcoholic solution was acidified with hydrochloric acid and the alcohol distilled off with steam. The hydrochloride solution was concentrated on a water bath. The hydrochloride — a thick, light-brown oil — was decomposed with powdered caustic soda. The resulting base was repeatedly extracted with absolute ether. The ether solution was dried with anhydrous caustic potash and fractionated. The ether was distilled off first, and three fractions were then collected: I) b.p. up to 56° at 6 mm — 0.72 g; II) b.p. 56-60° at 6 mm — 7.63 g; III) b.p. 69.5-140° at 9 mm — 1.42 g.

During the second fractionation, 7.02 g (i.e. 53.6%) of γ-butoxypropylamine resulted, b.p. 74-76° at 20 mm, 169-170° at 756 mm; n_D^{20} 1.4288; d_4^{20} 0.8532; MR_D 39.61; calculated 39.59.

8.280 mg substance: 0.793 ml N_2 (23°, 740 mm); 8.670 mg substance: 0.831 ml N_2 (21°, 738 mm). Found %: N 10.75, 10.81. $C_7H_{17}NO$. Calculated %: N 10.68.

Literature data: b.p. 75-76° at 21 mm; n_D^{20} 1.4273; d_{20}^{20} 0.8514 [22].

Hydrochloride. Obtained by passing dry hydrogen chloride into an ester solution of the amine. Very hygroscopic.

Picrate. Obtained by heating the base with a saturated benzene solution of picric acid. Yellow rhombohedrons with m.p. 96°. Soluble in water, methyl and ethyl alcohols.

Benzoyl Derivative. Obtained by the Shotten-Baumann reaction. Viscous, slightly yellow liquid, b.p. 192-195° at 3 mm.

Chloroplatinate. Golden scales from aqueous alcohol; m.p. 199° (decomp.).

Reduction of β,β'-Dicyandiethylsulfide

1.72 g (21.9% of theory) of γ-butoxypropylamine with b.p. 69-70° at 16 mm was isolated after reduction of 8.3 g of β,β'-dicyandiethylsulfide, obtained by the action of 18 g of metallic sodium in 270 ml of absolute butyl alcohol in the usual manner. Picrate — m.p. 96°. Melting point of the sample mixed with picrate obtained from the preceding experiment did not give depression. The remaining reduction products were not investigated.

Reduction of β-Alkoxypropionitriles

Reduction of β-Ethoxypropionitrile in Ethyl Alcohol (Method A). A heated solution of 14.1 g (0.14 mole) of β-ethoxypropionitrile in 250 ml of absolute ethyl alcohol was poured rapidly into 20 g of metallic sodium placed in a liter round-bottomed flask with horned adapter and heavy-duty copper reflux condenser. An oil bath preheated to 130-135° was placed immediately under the flask. This temperature was maintained until the sodium had completely dissolved. After termination of reaction, about 100 ml of water was added to the mixture while still warm, and the amine and alcohol were distilled off with steam into a receiver containing dilute hydrochloric acid, and then the acid solution of the hydrochloride was concentrated on a water bath. The hydrochloride, in the form of a viscous oil, was decomposed with solid caustic soda and repeatedly extracted with absolute ether. The ether solution was dried with anhydrous caustic potash and distilled in vacuo. Two fractions were collected: I) b.p. 54-55° at 39 mm — 6.95 g; II) b.p. 116-117° at 18 mm — 1.45 g.

The first fraction represented γ-ethoxypropylamine; n_D^{20} 1.4242; d_4^{20} 0.8697; MR_D 30.28; calculated 30.35.

Literature data: b.p. 134-136° at 732 mm; n_D^{20} 1.4201; d_4^{20} 0.8613 [22].

The high-boiling fraction — β-(β'-ethoxy)-propyltrimethylenediamine; n_D^{20} 1.4512; d_4^{20} 0.9040; MR_D 47.75; calculated 47.81.

Its picrate was obtained upon heating the amine with a benzene solution of picric acid. After recrystallization from benzene, m.p. 143°.

7.495 mg substance: 1.190 ml N_2 (22°, 752 mm); 5.587 mg substance: 0.880 ml N_2 (22°, 752 mm). Found %: N 18.18, 18.03. $C_{20}H_{26}O_{15}N_8$. Calculated %: N 18.12.

β-Isopropoxypropionitrile Reduction (Method B). 14 g of metallic sodium was dispersed in hot toluene (50 ml) with a mechanical stirrer in a three-necked flask equipped with reflux condenser and dropping funnel. Then, over a period of 15 minutes, with stirring, 11.3 g (0.1 mole) of β-isopropoxypropionitrile in 60 ml of absolute isopropyl alcohol was added. For the solution of all sodium, 40 ml more of alcohol was added. Further treatment was carried out in a manner identical with the isolation of γ-ethoxypropylamine.

2.52 g (21.5% of theory) of γ-isopropoxypropylamine resulted after fractionation of the base. B.p. 74-75° at 68mm. According to the literature data: b.p. 85-86° at 102 mm [22].

γ-Butoxypropylamine. Obtained in yield of 50% from reduction of β-butoxypropionitrile in absolute butyl alcohol: b.p. 80-81° at 24 mm.

By the same method β-isoamylhydroxypropionitrile was reduced in absolute isoamyl alcohol. There resulted from 14.1 g of the nitrile, 7.5 g of γ-isoamylhydroxypropylamine, with b.p. 82-83° at 20 mm; n_D^{20} 1.4312; d_4^{20} 0.8517; MR_D 44.17; calculated 44.21.

Picrate – from benzene; m.p. 104°.

6.703 mg substance: 0.882 ml N_2 (23°, 754 mm). 7.802 mg substance: 1.055 ml N_2 (24°, 755 mm). Found %: N 15.06, 15.11. $C_{14}H_{22}O_8N_4$. Calculated %: N 14.97.

Upon reducing 10.5 g (0.123 mole) of β-methoxypropionitrile in absolute butyl alcohol by method A, 4.15 g (25.8% of theory) of γ-butoxypropylamine with b.p. 69-70° at 18 mm resulted. Low-boiling fraction – 0.6 g of uncharacterized substances.

Upon carrying out by the same method, the reduction of 11.5g(0.1 mole) of β-(β'-hydroxyethoxy)-propionitrile in butyl alcohol yielded 3.85 g (29.4%) of γ-butoxypropylamine with b.p. 57-58° at 8 mm; n_D^{20} 1.4280; d_4^{20} 0.8538.

Melting point of a sample of the picrate mixture from the γ-butoxypropylamine of the last two experiments with the picrate of γ-butoxypropylamine obtained by reduction of β-butoxypropionitrile in butyl alcohol did not give depression.

Reduction of β-phenoxypropionitrile was carried out according to method B, in ethyl alcohol without stirring of the reaction mixture. During the treatment which was identical with isolation of the alkoxypropylamines, 5.72 g of γ-ethoxypropylamine with b.p. 59-60° at 48 mm (yield 55.5%) resulted, and 0.2 g of substance with b.p. 100-104° at 12 mm, the composition of which was not determined. The authors were not able to obtain any noticeable quantities of the base when they attempted to isolate γ-phenoxypropylamine by extraction of the aqueous-alkaline solution remaining after steam distillation.

β-Hydroxypropionitrile (Ethylenecyanhydrin) Reduction. A solution of 8.52 g (0.12 mole) of ethylenecyanhydrin in 180 ml of absolute ethyl alcohol was heated to boiling in a round-bottomed flask equipped with reflux condenser and horned adapter. 16 g of metallic sodium was then dropped into the solution in 2-3 g lots. After dissolution of the metal, the alcoholate was decomposed with water and distilled with steam. The acidified distillate was evaporated and the hydrochloride decomposed in the usual manner. 2.6 g of γ-ethoxypropylamine resulted, with b.p. 58-59° at 45 mm. Hydrogenated acrylic acid was not found in the alkaline residue from distillation with steam. To separate the propanolamine, this solution was placed in a flask with a low outlet tube and was distilled to dryness. 30-40 ml of water was then added and redistilled to dryness. This operation was repeated twice. The distillate was placed in a Favorsky flask with tall dephlegmator, and water distilled out at 110°. The residue, about 1.5 g of viscous liquid, was not a base and did not have a defined boiling point.

By reduction of ethylenecyanhydrin (10.7 g, i.e. 0.15 mole) with sodium (19 g) in isopropyl alcohol (290 ml) by method B, there resulted 3.26 g (20%) of γ-isopropoxypropylamine, b.p. 78-79° at 86 mm.

By reduction of ethylenecyanhydrin in isobutyl alcohol by method A, γ-isobutoxypropylamine resulted, in 24.4% yield; b.p. 65-66° at 20 mm; n_D^{20} 1.4246; d_4^{20} 0.8448; MR_D 39.63; calculated 39.59.

Picrate – m.p. 100° (from benzene).

8.595 mg substance: 1.184 ml N_2 (22°, 746 mm). 7.015 mg substance: 0.980 ml N_2 (22°, 746 mm). Found %: N 15.64, 15.67. $C_{13}H_{20}O_8N_4$. Calculated %: N 15.55.

An attempt to separate propanolamine from the reaction products also gave negative results.

Upon reducing ethylenecyanhydrin in n-butyl alcohol by the same method, the authors obtained γ-butoxypropylamine in 20% yield.

The ethylenecyanhydrin was reduced in isoamyl alcohol by Method B. 4.26 g (0.06 mole) of ethylenecyanhydrin and 13 g of sodium in 290 ml of absolute isoamyl alcohol were taken, i.e. one-and-a-half times more than in the preceding experiments. 3.17 g of γ-isoamylhydroxypropylamine (36.4% of theory) was separated; b.p. 66-67° at 12 mm.

Reduction of β-Chloropropionitrile. Reduction was carried out in n-butyl alcohol according to Method B. γ-Butoxypropylamine, b.p. 78-79° at 23 mm (68% of theory) and propyl amine in the form of the hydrochloride (8.4%) were separated during processing of the reduction products.

SUMMARY

1. It has been found that upon reducing β-halo-, β-hydroxy-, β-alkoxy- and β-thiopropionitriles according to the method of Vyshnegradsky (with sodium in alcoholic medium), an abnormal reaction takes place, which leads to formation of γ-alkoxypropylamines, while the alkoxy group becomes the radical of that alcohol in which medium the reduction is carried out.

2. The mechanism of this reaction has been investigated, and it has been proved that the process goes through a stage of acrylonitrile cleavage, with subsequent cyanethylation of the alcohol and reduction of the alkoxynitrile thus formed.

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THE MECHANISM OF OXIDATION AND NITRATION OF CYCLOHEXANE BY NITRIC ACID AND NITROGEN OXIDES. I

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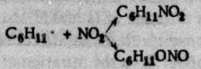
The oxidation and nitration of cyclohexane by nitric acid were investigated by Markovnikov [1], Nametkin [2] and Aschan [3]. From the point of view of classical organic chemistry, this reaction was most thoroughly studied by S. S. Nametkin.

The paraffin chain nitration theory developed by the author [4] made possible the determination of this reaction mechanism and discovery of new approaches. According to the author's theory, the initial stage of oxidation and nitration of cyclohexane, both by nitric acid and by nitrogen oxides, is the appearance of the free cyclohexyl radical during successful collisions of hydrocarbon with the radical monomer of nitrogen dioxide;

$$C_6H_{12} + NO_2 \longrightarrow C_6H_{11}\cdot + HNO_2. \qquad (1)$$

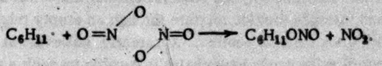
Further, the principal transformation of cyclohexane in the nitration zone can be represented by Reactions 2-5:



$$C_6H_{11}\cdot + NO_2 \longrightarrow C_6H_{11}NO_2 \qquad (2)$$

$$C_6H_{11}\cdot + NO_2 \longrightarrow C_6H_{11}ONO \qquad (3)$$

$$C_6H_{11}\cdot + N{=}O \longrightarrow C_6H_{11}N{=}O, \qquad (4)$$



$$C_6H_{11}\cdot + O{=}N\overset{O}{\diagup}\quad \underset{O}{\diagup}N{=}O \longrightarrow C_6H_{11}ONO + NO_2. \qquad (5)$$

During nitration in the liquid phase at elevated temperatures, the significance of directions (4) and (5) will be small, with a few exceptional cases, and consequently the principal primary reaction products will be nitrocyclohexane and cyclohexylnitrite. Nitrocyclohexane should survive as a final reaction product, and cyclohexylnitrite, through intermediate formation of cyclohexanol, should be transformed into a mixture of adipic and lower dicarboxylic acids.

According to the author's theory, nitric acid should not exert independent oxidizing and nitrating actions. It affects the rate and the ratio between the principal direction of the reaction only through its participation in the equilibrium $2HNO_3 + NO \rightleftarrows 3NO_2 + H_2O$, which serves as the source and the means for progressive regeneration of nitrogen dioxide from the lower oxides. At high temperatures, the pyrolysis products of nitric acid: nitric anhydride, nitrogen trioxide, NO_3, NO_2, and so forth, may prove to be active. Experiments confirmed these deductions from the general nitration theory of the paraffinic chain. It was first of all demonstrated that cyclohexane reacts noticeably with nitrogen dioxide at normal temperature, and comparatively rapidly at 100°. Under appropriate conditions, the reaction leads to the formation of adipic acid and nitrocyclohexane for the most part, i.e., the same products as from the interaction of cyclohexane with nitric acid.

Furthermore, by carrying out the reaction with nitric acid under the same conditions as with nitrogen dioxide, and also according to the S. S. Nametkin method, the authors have proved that interaction almost ceases in the absence of nitrogen dioxide in the reaction zone, and the rate of its reaction was found to be proportional to the addition of NO_2. Moreover, during oxidation by nitrogen dioxide, the addition of nitric acid in the corresponding cases affected reaction yields negatively, due to the presence of water in the acid used and due to a shift to the right of the equilibrium $3NO_2 + H_2O \rightleftarrows 2HNO_3 + NO$.

The reaction course in the gaseous phase, through interaction of cyclohexane with nitrogen dioxide, has been established by its accomplishment in sealed tubes at 100° by heating of the hydrocarbon and nitrogen dioxide mixture taken in such quantities as to ensure their complete vaporization. The absence of the oxidizing and nitrating action of nitric acid under these conditions results from nitration according to Nametkin, by the addition of ammonium sulfate, since the reaction is capable of occurring in the gaseous phase because the tubes were not more than one-third full.

Experimental proof of the absence of reaction between nitric acid and hydrocarbons at high temperature ($> 200°$) is extremely difficult to obtain due to the simultaneous self-decomposition of the nitric acid to form nitrogen dioxide. Moreover, it cannot be denied that at sufficiently high temperature the direct interaction of nitric acid with the paraffin chain may become noticeable; even more probable are reactions with pyrolysis products HNO_3–N_2O_5, $NO_3·$, $·NO_2$, etc. And also, all of the experiments carried out at 320-340° demonstrated that the yields of reaction product upon interaction of cyclohexane with nitrogen dioxide were almost ten-fold greater than with analogous experiments using nitric acid of sp. gr. 1.4. With an increase in the duration of nitric acid remaining in the reaction tube, the yield of reaction product increased somewhat, which is explained by the increased possibility of its decomposition. These results at least indicate a low reaction rate with nitric acid, even at temperatures this high.

The radical character of the primary reaction between cyclohexane and nitrogen dioxide [1] is confirmed by various experimental data. This indicates possibility of its existence in the gaseous phase. There is practically no change in the reaction yield with increase in the quantity of nitric acid, and the large increase in reaction yield with an increase in the quantity of cyclohexane demonstrates its role in the hydrocarbon phase, which is also in agreement with the accepted radical character of the reaction. The absence of any noticeable acceleration of reaction between nitrogen dioxide and cyclohexane upon adding strong protonic and aprotonic acids — sulfuric acid, aluminum chloride, titanium tetrachloride and also iodine — indicates the insignificant role of the ionic character of interaction in the primary oxidation and nitration stage of the paraffinic chain.

The above-indicated traits are characteristic for nitration of cyclohexane, and are entirely different for the parent substance of aromatic compounds — benzene, with which there is a genetic relation. This corresponds to the general distinctions which are made between the nitration of saturated and of aromatic hydrocarbons, and the mechanisms accepted for them [5]. In agreement with the position indicated, the authors also found that the addition of mercury salts had little noticeable effect upon the nitration of cyclohexane.

In accordance with the adopted mechanism, the nitration and oxidation reaction of cyclohexane does not possess a chain character. This deduction was confirmed by the observation that there was no difference in reaction rates upon passing cyclohexane and nitrogen dioxide mixture through an empty tube in one experiment as against passing through a tube filled with glass chips in another. Apparently, however, at high concentration of nitrogen dioxide dimer, the development of sufficiently long chains is possible by such a scheme:

$$R{-}H + NO_2^{\bullet} \longrightarrow R\cdot + HNO_2,$$

$$R\cdot + N_2O_4 \longrightarrow RONO + NO_2^{\bullet},$$

$$NO_2^{\bullet} + R{-}H \longrightarrow R\cdot + HNO_2, \text{etc.}$$

The breaking of chains will occur at the expense of combination of radicals with NO and NO_2, branching at the expense of the side reactions of cyclohexylnitrite and cyclohexanol oxidation. It is very probable that such a case was realized experimentally by the authors when, upon heating 0.84 g of cyclohexane and 4.5 g of nitrogen dioxide in a sealed tube at 100°, the tube exploded with considerable shattering effect.

EXPERIMENTAL

The procedure for treatment of the nitration and oxidation product of cyclohexane was carried out according to the following method, with the following, or other, minor modifications. The reaction mass, which normally contained solid adipic acid, was filtered off with suction; the precipitate was washed with small quantities of cyclohexane and water, and after being dried in air, represented quite pure adipic acid with m.p. about 151°. The aqueous portion of the filtrate was evaporated to dryness on a water bath. The mixture of adipic, glutaric, succinic and oxalic acids which resulted from such procedure normally melted at 130-140°, but still consisted for the most part of adipic acid since it gave an increased melting point upon heating with the pure product. All of the cyclohexane was distilled off from the organic layer of the filtrate after washing with soda solution. The remaining crude nitro product, the greater portion of which redistilled at 20 mm pressure with a b.p. of 95-100°, had n_D^{20} 1.463 and possessed other properties approximating those for pure nitrocyclohexane. The authors observed that its dissolution in alkali was speeded up by additions of diethylamine, although not to such striking extent as was found earlier for phenylnitromethane.

Comparison of the Behavior of Cyclohexane With Nitrogen Dioxide and Nitric Acid.

a) Experiments at Normal Temperature in Sealed Tubes. A mixture composed of 10 ml of cyclohexane and 10 ml of nitric acid, sp. gr. 1.4, not containing any nitrogen oxides, in the first experiment, and a mixture composed of the same quantity of hydrocarbon with 6 g of nitrogen dioxide in the second experiment, were left standing for 60 days in sealed tubes at 20-25°. No excess pressure was found upon opening the tube containing the nitric acid. Only traces of nitro products were isolated, formed possibly at the expense of nitrogen oxides that developed at random. A very high pressure was found in the second tube, and from the reaction product 0.20 g of nitrocyclohexane and 2.37 g of adipic acid — 65% of the theoretical yield, resulted.

b) Experiments at 60° in an Open Container. The reaction with nitrogen dioxide was carried out in a three-necked flask. A mixture of 20 g of nitrogen dioxide and 50 ml of hydrocarbon was added to 350 ml of cyclohexane over a period of 16 hours, and with simultaneous passing through of 3 liters of oxygen. 5.1 g of adipic acid and 6.7 g of crude nitrocyclohexane were isolated from the reaction mixture.

Upon treatment of the nitroproduct with 10% KOH solution and with addition of diethylamine, with subsequent recrystallization of the undissolved residue from alcohol, there resulted a small quantity of colorless, crystalline substance with m.p. 216°. As melting of a mixed sample indicated, the substance isolated was apparently 1,1'-dinitrodicyclohexyl, obtained earlier by S. S. Nametkin, according to his method, during the nitration of cyclohexane.

The experiment carried out under the same conditions, but with application of 40 ml of nitric acid, sp. gr. 1.4, and with addition of 2 g ammonium nitrate instead of nitrogen dioxide, gave only traces of reaction products.

TABLE 1

Expt. No.	Additions	Obtained (g)	
		$C_4H_8(COOH)_2$	$C_6H_{11}NO_2$
1	—	1.2	0.8
2	1 g $(NH_4)_2SO_4$	—	Traces
3	1 g N_2O_4	1.8	1.6

TABLE 2

Expt. No.	Taken into reaction		Obtained (g)		Total yield (a + b) (in mole · 100)
	HNO_3 (ml)	N_2O_4 (g)	$C_4H_8(COOH)_2$ (a)	$C_6H_{11}NO_2$ (b)	
1	10	0.9	0.59	0.08	0.465
2	10	2.8	1.33	0.15	1.027
3	—	2.8	1.05	0.41	1.038

TABLE 3

Expt. No.	C_6H_{12} (in g)	Yield (in g)		Total yield (in mole · 100)	HNO_3 consumption (in %)
		$C_4H_8(COOH)_2$	$C_6H_{11}NO_2$		
1	0.21	0.03	Traces	0.020	0.68
2	0.42	0.10	Traces	0.068	2.23
3	0.84	0.25	Traces	0.169	5.80
4	1.68	0.59	0.08	0.466	14.20
5	3.36	1.76	0.98	1.940	48.50
6	5.23	1.92	1.73	2.520	58.0
7	9.24	2.36	2.05	3.170	70.30

c) Experiments in Sealed Tubes at 100°. 10 ml of cyclohexane was mixed in one case with 2 ml of nitrogen dioxide, and in the other — with 10 ml of nitric acid, spec. grav. 1.3, and with addition of 1 g ammonium sulfate, added to remove nitrogen oxides that might appear. The two mixtures were heated in sealed tubes at 100° for 3 hours.

1.08 g adipic acid and 2.00 g of crude nitrocyclohexane containing, as further investigation showed, a noticeable quantity of cyclohexylnitrite, were isolated from the cyclohexane + nitrogen dioxide reaction mixture. In the nitration experiment, almost no interaction of nitric acid occurred.

d) Experiments at Normal Pressure and at 320-330° in the Gaseous Phase (See [6]). Oxidation and nitration of cyclohexane by nitric acid was carried out with and without the presence of nitrogen dioxide. The first experimental series was carried out according to the method of S. S. Nametkin. One experiment was carried out in exact accordance with the literature directions, the second — with addition of ammonium sulfate to remove traces of nitrogen oxides contained in the normal nitric acid and which might appear during the reaction, and finally, the third — with preliminary addition of nitrogen dioxide. The basic charge for each of the tubes consisted of 10 ml of cyclohexane and 15 ml of nitric acid, sp.gr. 1.2. Heating of the sealed tubes was carried out in a horizontal oven at 103-107° for a period of 9 hours, during which, at two hour intervals, the excess pressure was let out. Data are given in Table 1.

In the second experiment — without nitrogen oxides — excess pressure was not found; the appearance of traces of nitroproducts can be explained by the impossibility of inhibiting the formation of small amounts of nitrogen oxides in the cyclohexane layer.

The effect of nitrogen dioxide quantity upon the reaction yield can be seen from the following series of experiments. The charge placed in each of the tubes consisted of 1.68 g of cyclohexane, varying quantities of nitric acid, sp.gr. 1.3, and nitrogen dioxide. Heating time in the horizontal water bath was 3 hours (Table 2).

The yield increased proportionately to the quantity of added nitrogen dioxide. In the third experiment (without addition of nitric acid) it was somewhat higher than in the similar experiment with addition.

Reaction in the Gaseous Phase at 100°. 0.5 g cyclohexane and 1.4 g of nitrogen dioxide were placed in a tube of 120 ml volume, so calculated that at 100° the substances taken for reaction would be completely converted to the gaseous state. After sealing and heating at 100° for 3 hours, there resulted 0.21 g of adipic acid and 0.04 g of nitroproduct.

Concerning the reaction course at 320-340°, see [6].

Effect of Quantity of Cyclohexane upon the Reaction Yield. The charge for each tube consisted of 10 ml of nitric acid, sp.gr. 1.3 (47.5%), 0.9 g of nitrogen dioxide and variable quantities of cyclohexane. Heating of the sealed tubes was carried out in a horizontal water bath for 3 hours (Table 3).

The extent of nitric acid consumption was calculated according to the stoichiometric equations:

$$3C_6H_{12} + 10HNO_3 = 3C_4H_8(COOH)_2 + 8H_2O + 10NO$$

and

$$C_6H_{12} + HNO_3 = C_6H_{11}NO + H_2O.$$

Taking into account the formation of lower dicarboxylic acids and CO_2, it should be considered that the true consumption of nitric acid was somewhat higher. The calculations indicate that in the first two cases reactions proceeded exclusively in the gas phase.

Investigation of the Action of Protonic and of Non-Protonic Acids. Addition of titanium tetrachloride, aluminum chloride and sulfuric acid to cyclohexane and nitrogen dioxide mixture caused no observable change. Nor was there found any accelerating effect by sulfuric acid additions to the cyclohexane-nitric acid mixture.

To test the actions of similar types of addition in relation to time, experiments were arranged with a mixture of 25 ml of cyclohexane and 6 g of nitrogen dioxide, to one portion of which was added 5 g of aluminum chloride, and to the other 2 g of iodine. Judging from the color intensity of nitrogen dioxide in the gaseous phase for the control experiment and in the test experiment upon adding aluminum chloride, the reaction rates in both experiments were very similar. Treatment of the reaction mixtures of the control and of the experimental tests after one month standing at normal temperature gave in all cases almost identical yields of reaction products — about 0.7 g of nitroproduct and the same quantity of adipic acid.

A rapid nitration course was observed by the authors during reaction of nitric anhydride with cyclohexane. The cyclohexane reaction, carried out with nitric acid in the presence of nitrogen dioxide in sealed tubes at 100° with additions of mercury nitrate indicated no effect for the latter.

SUMMARY

1. The interaction of cyclohexane with nitrogen dioxide proceeds with relative rapidity and gives the same products as nitration with nitric acid according to the method of Konovalov-Nametkin.

2. Oxidation and nitration of cyclohexane by nitric acid proceeds by way of an intermediate reaction with nitrogen dioxide.

3. The radical character of the primary reaction stage has been confirmed by its course in the gaseous and hydrocarbon phases, and by the absence of any accelerating action of strong protonic, aprotonic acids, or mercury salt additions upon it.

4. The nitration theory for the paraffinic chain, as earlier developed, is applicable to the oxidation and nitration of cyclohexane.

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THE REACTIONS OF ALIPHATIC DIAZO COMPOUNDS WITH UNSATURATED COMPOUNDS

XIV. REACTION OF DIAZOACETATE WITH HALOGEN DERIVATIVES OF THE ALIPHATIC-AROMATIC SERIES.

I. A. Dyakonov and N. B. Vinogradova

As was demonstrated earlier [1-3], halogen derivatives of hydrocarbons of the allyl type react with diazoacetate in the presence of copper catalyst according to the equation (1):

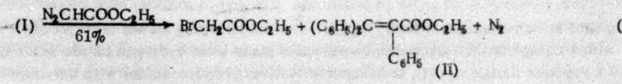
$$RX + N_2CHCOOC_2H_5 \xrightarrow[(CuSO_4)]{Cu} RCHXCOOC_2H_5 + N_2, \qquad (1)$$

where, for the examples investigated, R = Radical of $CH_2{=}CH{-}CH_2{-}$, and X = Cl, Br or I.[*] Since it was found that halogen derivatives of the non-allyl type (ter- and n-butyl bromides) do not readily enter into reaction [3], an attempt has been made to expand this reaction to include halogen derivatives of hydrocarbons of the aliphatic-aromatic series which possess a more mobile halogen atom: benzyl bromide, di- and tri-phenylbromomethanes.

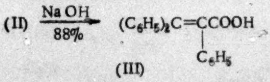
The results of these experiments are described in the present article.

Investigation has shown that the reaction course for experiments with triphenylbromoethanes in the presence of copper sulfate as catalyst, and ligroin as diluent, may be expressed by equations (2) and (3):

$$(C_6H_5)_3CBr \xrightarrow[CuSO_4]{N_2CHCOOC_2H_5} \underset{(I)}{(C_6H_5)_3CCHBrCOOC_2H_5} + N_2; \qquad (2)$$



$$(I) \xrightarrow[61\%]{N_2CHCOOC_2H_5} BrCH_2COOC_2H_5 + \underset{(II)}{(C_6H_5)_2C{=}\underset{C_6H_5}{\underset{|}{C}}COOC_2H_5} + N_2 \qquad (3)$$



$$(II) \xrightarrow[88\%]{NaOH} \underset{(III)}{(C_6H_5)_2C{=}\underset{C_6H_5}{\underset{|}{C}}COOH} \qquad (4)$$

The final reaction product expected in this case — the ethyl ester of β,β-diphenyl-α-bromohydrocinnamic acid (I) — was not separated from the reaction mixture: in the course of the synthesis, under the action of non-reacted diazoacetate, it immediately converted into the ester of triphenylacrylate (II) by splitting off HBr with rearrangement of the phenyl.[**] The evolving hydrogen bromide became bound with the diazoacetate to form bromoacetate.

With a 1:1 molar ratio for the reactants, in ligroin, the yield of analytically-pure ester (II) was 60.9%, and the yield of bromacetate was 60.8% of the theoretical, calculating on the basis of original diazoacetate, and taking into account the combined equation resulting from equations (2) and (3).

The ester (II) was converted into triphenylacrylic acid (III) in 88% yield by the action of alkali. The yields of ester (II) cited in the literature are small [7], in connection with which it should be noted that the reaction described here may have a preparative value for its synthesis [and likewise for synthesis of acid (III).]

As the result of the same reaction course (2) in the absence of solvent, and at a temperature of 160-165°, there were obtained: the bromacetate, 1,1,2-triphenylbutene-1 (V) and diphenylindone (IV) (yields respectively 81.2, 78.0 and 4-5%).[***]

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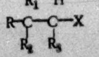
[*] The reaction, upon which is based the diazo method for synthesis of simple organic compounds, is analogous to that quoted above (1) [4]. In Group IV, e.g. the halogenides of Si, Sn and Pb react in the indicated manner. In 1951 the authors [1], and a little later some American chemists [5], demonstrated that this reaction can also be extended to include certain halogen derivatives of hydrocarbons of the aliphatic series.

[**] Rearrangement upon splitting off HX from halogen derivatives of the general formula

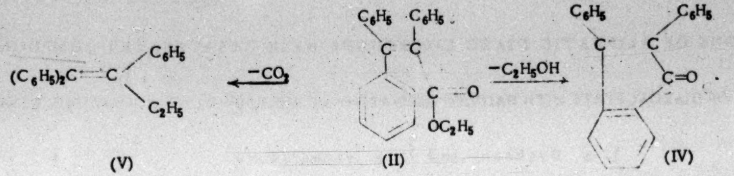


$$R{-}\overset{R_1}{\underset{R_2}{C}}{-}\overset{H}{\underset{R_3}{C}}{-}X$$

have been adequately studied [6].

[***] According to calculation for 0.5 mole of initial diazocetate.

The formation of compounds (IV) and (V) may be explained in the following manner. Under the conditions of the experiment, at a temperature of 160-165°, ester (II), which at first is formed primarily according to Equations (2) and (3), decomposes in two ways:

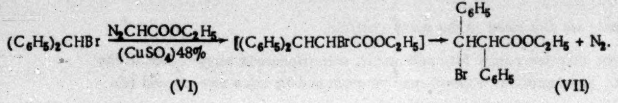


(5)

It is known from the literature data that diphenylindone actually forms as a side product in the synthesis of ester (II) at the expense of its partial intramolecular condensation [8].

Unknown up to the present time, hydrocarbon (V) is apparently formed also upon decomposition of the ester (II), because it was possible to find (qualitatively) CO_2 in the nitrogen evolving during the condensation reaction. This secondary reaction was not investigated in any more detail.

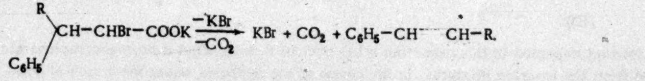
Condensation of diphenylbromethane with diazoacetate was carried out with a 1:1 molar ratio of reactant in the presence of cupric sulfate and in the absence of solvent, at a temperature of 80°. The reaction product corresponded in composition to the β-phenyl-α-bromhydrocinnamic acid ester (VI); however, further investigation has shown that it has the structure of the isomeric α-phenyl-β-bromhydrocinnamate (VII):



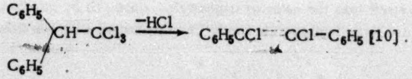
$$(C_6H_5)_2CHBr \xrightarrow[(CuSO_4)48\%]{N_2CHCOOC_2H_5} \underset{(VI)}{[(C_6H_5)_2CHCHBrCOOC_2H_5]} \rightarrow \underset{(VII)}{\overset{C_6H_5}{\underset{Br}{C}}H\underset{C_6H_5}{C}HCOOC_2H_5} + N_2. \qquad (6)$$

The authors are inclined to think that during the course of the reaction there occurs isomerization of the unstable normal reaction product (VI) into the more stable isomer (VII) with a symmetrical distribution of the phenyl groups.

The possibility of a similar isomerization of ester (VI) indicates the following known facts for other compounds. Rearrangements, with a change in the carbon framework, takes place when hydrogen halide acids split out from the esters which have a structure similar to (VI), or halogen derivatives of hydrocarbons with unsymmetrical distribution of phenyl groups (where R = C_6H_5, C_2H_5 [9]):



$$\begin{matrix} R \\ C_6H_5 \end{matrix}\!\!>CH-CHBr-COOK \xrightarrow[-CO_2]{-KBr} KBr + CO_2 + C_6H_5-CH=CH-R.$$



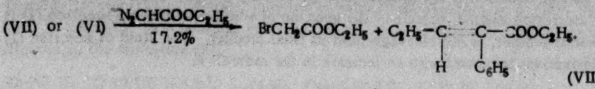
$$\begin{matrix} C_6H_5 \\ C_6H_5 \end{matrix}\!\!>CH-CCl_3 \xrightarrow{-HCl} C_6H_5CCl=CCl-C_6H_5 \text{ [10]}.$$

Halogen derivatives of the hydrocarbons of the aliphatic series isomerize with migration of the halogen atom within the carbon chain (A. E. Favorsky [11]) and sometimes irreversibly with a change in the carbon framework [12]:

$$(CH_3)_2CH-CH_2Br \overset{180\text{-}200°}{\rightleftarrows} (CH_3)_3CBr \xrightarrow{\geq 200°} CH_3-CHBr-CH_2-CH_3.$$

It is quite possible that isomerization in the halogen derivative series of aliphatic-aromatic hydrocarbons will occur at lower temperature than in the aliphatic series (in our case – at 80°).

Ester (VII) is described here for the first time. Yield = 31.2% of theoretical for crude product with m.p. 110° (possibly a mixture of 4 diazostereoisomers) and 20.1% for the product with a constant m.p. of 132°. Since the bromacetic acid ester was also isolated from the reaction, and, after alkaline treatment, a small quantity of the acid corresponding to ester (VII), then it should be assumed that in this case a secondary reaction has been substituted for that of the diazoacetate with the bromoester (VI) or (VII):



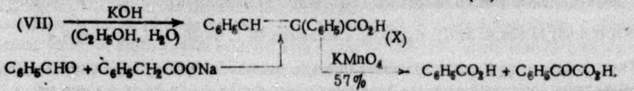
$$(VII)\ \text{or}\ (VI) \xrightarrow[17.2\%]{N_2CHCOOC_2H_5} BrCH_2COOC_2H_5 + C_2H_5-\underset{H}{C}=\underset{C_6H_5}{C}-COOC_2H_5. \qquad (7)$$

(VIII)

For determination of the structure of ester (VII), which at first was taken to be ester (VI), it was treated with alcoholic caustic alkali. Here, instead of the β -phenylcinnamic acid (IX), there was obtained the trans-α-phenylcinnamic acid (X).

With view in mind of the possibility of rearrangement upon the HBr cleavage reaction, the authors attempted to replace bromine by hydroxyl in the ester investigated, by reaction with aqueous rather than alcoholic alkali. However, instead of the β,β-diphenyllactic acid (XI) which was expected here, acid (X) again resulted. For proof of the structure, the latter was first oxidized with potassium permanganate, at which time benzoic and benzoylformic acids resulted, and were identified by mixed sample test with known acid (from benzaldehyde and sodium phenylacetate [13]).

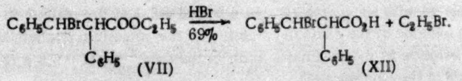
$$\underset{(IX)}{(C_6H_5)_2C=CHCOOH} \xleftarrow[(C_2H_5OH)]{KOH} (VI) \xrightarrow[(H_2O)]{KOH} \underset{(XI)}{(C_6H_5)_2CHCHOHCOOH}. \qquad (8)$$



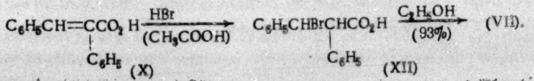
$$(VII) \xrightarrow[(C_2H_5OH,\ H_2O)]{KOH} C_6H_5CH=C(C_6H_5)CO_2H\ (X) \xrightarrow[57\%]{KMnO_4} C_6H_5CO_2H + C_6H_5COCO_2H. \qquad (9)$$

$$C_6H_5CHO + C_6H_5CH_2COONa \longrightarrow (X)$$

The obtaining of acid (X) cannot be considered faultless proof of the bromester structure. For determination of the structure, it is necessary to select a reaction which will not affect the rearrangement centers , i.e., the C-Br and C-H bonds in the molecule of this compound. The dealkylation reaction of the ester by the use of a strong HBr solution in glacial acetic acid was found to be suitable for this purpose. The α-phenyl-β-bromhydrocinnamic acid (XII) isolated as the result of the dealkylation, had a m.p. of 185° [13], in contrast to its isomeric form, β-phenyl-α-bromhydrocinnamic acid (with m.p. 164° [9]), and displayed all of the reactions characteristic for it. A sample of known acid (XII) was obtained (according to Müller [13]), for comparison, by reacting concentrated HBr with α-phenyl-cinnamic acid (X), and finally by esterification of the acid (XII) there was obtained the corresponding ethyl ester which was found to be identical with the ester (VII):



$$C_6H_5CHBr\underset{C_6H_5}{C}HCOOC_2H_5\ (VII) \xrightarrow[69\%]{HBr} C_6H_5CHBr\underset{C_6H_5}{C}HCO_2H\ (XII) + C_2H_5Br. \qquad (10)$$



$$C_6H_5CH=\underset{C_6H_5}{C}CO_2H\ (X) \xrightarrow[(CH_3COOH)]{HBr} C_6H_5CHBr\underset{C_6H_5}{C}HCO_2H\ (XII) \xrightarrow[(93\%)]{C_2H_5OH} (VII). \qquad (11)$$

The yield of acid (XII) (crude product) by dealkylation, and of the ester (VII) from the esterification reaction, constituted, respectively, 69 and 93% of the theoretical yields. The reactions expressed by Equations (10) and (11) finally determined the structure of the ester (VII).

Benzyl bromide apparently reacts only to a small extent with the diazoacetate in the direction expected:

$$C_6H_5CH_2Br \xrightarrow[(Cu)]{N_2CHCOOC_2H_5} \underset{(XIII)}{C_6H_5CH_2CHBrCOOC_2H_5} + N_2. \qquad (12)$$

The reaction is accompanied by formation of a considerable quantity of fumarate due to decomposition of unconsumed diazoacetate, and also by large amounts of tars.

A number of attempts to isolate the ester (XIII) from the resinous reaction product, or to prove its presence in it by the use of various reactions, was to no avail. Only dehalogenating reduction with Zn dust in acetic acid led to the isolation of a small quantity of ethyl hydrocinnamate (XIV), which was identified with the known by the hydrazide of the acid:

$$(XIII) \xrightarrow{Zn + CH_3COOH} \underset{(XIV)}{C_6H_5CH_2CH_2COOC_2H_5} \xrightarrow{NH_2NH_2} \underset{(XV)}{C_6H_5CH_2CH_2CONHNH_2}. \qquad (13)$$

This result allows us to assert that Reaction (12) can be considered proved in principle.

It should be considered that an equation of the general form (1) [$R = C_6H_5CH_2$; $(C_6H_5)_2CH$; $(C_6H_5)_3C$; $X = Br$] encompasses all three types of interaction studied, outside of the question of whether additional reaction (1) is accompanied by isomerization, rearrangement, or HBr cleavage from its final product. The yield of Reaction (1) in a series of investigated halogen derivatives increased with an increase in the radical R.

EXPERIMENTAL

I. Condensation with Triphenylbrommethane in Ligroin. For a description of the apparatus (see [1-3]). 32.2 g of triphenylbrommethane [14] 100 ml of purified ligroin (b.p. 100-110°) and 0.2 g of anhydrous $CuSO_4$ were heated until the greater portion of triphenylbrommethane went into solution. After that 11.4 g of diazoacetate was added dropwise to the boiling solution with mechanical stirring.* 3.2 liters of nitrogen were evolved (15°, 758.8 mm).

The reaction mixture was filtered from the catalyst while hot. Upon cooling, the filtrate crystallized. The crystals were removed by suction and the ligroin mother liquor was further fractionated.

Ethyl Triphenylacrylate (II). After recrystallization from alcohol, 10 g (60.9% of the theoretical yield, calculated on the basis of diazoacetate) of crystals of almost colorless ester (II) resulted, with a m.p. of 119-120°. The ester gave with concentrated H_2SO_4 a characteristic green color, changing to ruby-red upon heating. The melting point and other properties corresponded to that indicated in the literature [15].

Found %: C 83.97; H 6.03; M 324.4, 317.1. $C_{23}H_{20}O_2$. Calculated %: C 84.10; H 6.14. M 328.4.

Bromacetate. Upon fractionating the ligroin mother liquor, a fraction of the substance with lachrymatory properties and with a boiling point corresponding to the bromacetate was obtained. Yield 18.2 g (60.8% of theoretical).

B.p. 156-161°; d_4^{18} 1.492; n_D^{18} 1.452.

Found %: Br 46.38. $C_4H_7O_2Br$. Calculated %: Br 47.90.

Literature data [16]: b.p. 159°; d_4^{13} 1.514; n_D^{13} 1.454.

Certain deviations in the analytical data between found and calculated should be attributed to the possible impurity of fumarate (See [2]).

Triphenylacrylic Acid (III). 1 g of the ester (II) was heated for 8 hours with 16.5 g of caustic potash dissolved in 70 ml of alcohol. The solution was diluted with water, the alcohol distilled off, and the residue in the distilling flask was diluted with water to 100 ml because of the difficult solubility of the potassium triphenylacrylate. The free acid (III) was separated from the solution by dilute sulfuric acid, in the cold. Yield – 0.8 g (87.9% of theoretical). B.p. 212-213°– which corresponds to the literature [8].

Found %: C 83.77; H 5.73; equiv. (by titration) 299.3, 302.8. $C_{21}H_{16}O_2$.
Calculated %: C 83.99; H 5.37; equiv. 300.3.

II. Condensation with Triphenylbrommethane in the Absence of Solvent. 18.5 g of diazoacetate was added dropwise with mechanical stirring to 52 g of triphenylbrommethane and 0.2 g of anhydrous copper sulfate, heated at 160-165°. 5.2 liters of nitrogen was evolved (19°, 759.2 mm), which exceeded the theoretically required amount by 22%. The excess was attributed to the presence of carbon dioxide in the nitrogen, which was qualitatively determined by the use of baryta water. The reaction product (bromacetate) possessed considerable lachrymatory properties. It did not crystallize upon standing in the cold. After distilling off the bromacetate in vacuo (b.p. 50-60° at 11 mm, yield 11 g or 81.2% of the theoretical), there was obtained from the residue a dark, resinous mass which crystallized from a mixture of benzene and petroleum ether. After repeated crystallizations from benzene, and then from alcohol, 18 g of 1,1,2-triphenylbutene-1 (V) resulted, with m.p. 91-92° (78% of the theoretical yield). On concentrating the benzene-petroleum mother liquor from hydrocarbon (V), about 1 g of diphenylindone (IV) resulted.

1,1,2-Triphenylbutene-1 (V). Colorless needle crystals (from alcohol). m.p. 91-92°. Poorly soluble in cold conc. H_2SO_4, with formation of a green color, changing upon heating into an intense yellow.

0.0916 g, 0.0998 g substance: 0.3127 g, 0.3402 g CO_2: 0.0551 g, 0.0594 g H_2O. 0.2989 g, 0.4060 g substance: 13.62 g, 19.00 g C_6H_6 : Δt 0.40, 0.78°. Found %: C 92.11, 92.96; H 6.73, 6.98; M 281.5, 295.3 $C_{22}H_{20}$. Calculated %: C 92.90; H 7.09; M 284.4.

* The diazoacetate was purified beforehand by steam distillation in vacuo.

Diphenylindone (IV). Crystals, ruby-red in color (from alcohol), m.p. 150°. Gave a green coloration with conc. H_2SO_4 in the cold; upon heating, an orange color. The melting point and other properties corresponded to those indicated in the literature [8].

Found %: C 89.19; H 4.87. $C_{21}H_{14}O$. Calculated %: C 89.33; H 4.96.

III. Condensation with Diphenylbrommethane. 119.2 g of diphenylbrommethane [17] and 0.3 g of anhydrous $CuSO_4$ was heated to 80° and with mechanical stirring 55 g of diazoacetate was added to the mixture dropwise. 9.2 liters of nitrogen was evolved (17°, 764 mm). ..). The hot reaction mixture was filtered off from the catalyst, and crystals of the crude ester (VII) separated out from the filtrate upon standing in a desiccator, m.p. 110°, weighing 50.1 g (31.2% of the theoretical yield). A considerable portion of the ester (VII) remained apparently in the mother liquor along with products of a resinous character (see below).

Ethyl β-Brom-α-phenylhydrocinnamate (VII). The crude sample was purified by crystallization from alcohol-benzene mixture Colorless, light flaky crystals with m.p. 132°. Soluble in alcohol, benzene, ligroin, petroleum ether. Yield of pure sample was 32.3 g or 20.1 % of theoretical.

0.1161 g, 0.1538 g substance: 0.0650 g, 0.0867 g AgBr. 0.1085 g, 0.3775 g substance; 17.06 g, 25.78 g C_6H_6: Δt 0.10, 0.24°. Found %: Br 23.82, 24.00; M 326.3, 346.8. $C_{17}H_{17}O_2Br$. Calculated %: Br 23.98; M 333.22.

Investigation of the Mother Liquor. Bromacetate. The mother liquor remaining after separation of the ester (VII) crystals possessed a sharp lachrymatory odor. As the result of vacuum fractional distillation, 14 g (17.2% of the theoretical yield) of bromacetate resulted with a m.p. of 155-162°, along with 20 g of resinous, non-distillable residue. After repeated distillations, the bromacetate possessed the following constants: b.p. 158-159° and n_D^{20} 1.451 [16]. The resinous residue was boiled with a solution of alcoholic alkali (42 g of KOH in 170 ml of alcohol); the resulting homogeneous solution, dark in color, was diluted with water and acidified with sulfuric acid. The resinous acids separated from the residue were purified by crystallization from alcohol with subsequent reprecipitation. 4.3 g of colorless crystals of pure α-phenylcinnamic acid (X) with m.p. 172° resulted. A sample mixed with known sample (X) (m.p. 172°), prepared by the action of the Na salt of phenylacetic acid upon benzaldehyde [13], did not show depression.

α-Phenylcinnamic Acid; A) Ester (VII) and Alcoholic Alkali. 2 g of ester (VII) was heated with 2 g of KOH solution in 50 ml of alcohol. The alcohol was distilled off in vacuo, the residue dissolved in 100 ml, and the solution acidified with dilute sulfuric acid. From the solution colorless crystals of the acid (X) precipitated out, with m.p. 169°. Yield – 1.3 g (96.6% of theoretical). After crystallization from benzene, m.p. was 171-172°. A sample mixed with authentic sample of Acid (X) prepared as indicated above, did not show depression.

B) Ester (VII) and Aqueous Alkali. Hydrolysis of 3.3 g of ester (VII) with 20 ml of 10% aqueous caustic potash by boiling, and subsequent acidification of the alkaline solution gave 2.15 g (96.8% of the theoretical yield) of acid (X), with m.p. 169°. After crystallization from benzene, m.p. was 171-182°.

In conformity with the literature data [13], the acid (X) discolored potassium permanganate solution, did not add bromine in chloroform, and sublimed. Below are given data on the analysis of acid (X), and of the silver salt derived from it.

Found: equiv. 223.1, 224.7; OH 1.059, 0.984. $C_{15}H_{12}O_2$. Calculated: equiv. 224.3; OH 1.0. 0.2982 g, 0.1591 g salt: 0.0979 g, 0.0527 g Ag. Found %: Ag 32.83, 33.12. $C_{15}H_{11}O_2Ag$. Calculated %: Ag 32.62.

C) Oxidation of Acid (X). 2 g of acid (X) was dissolved in soda and oxidized in the cold with 2% $KMnO_4$ (3.6g). After the usual treatment, the aqueous solution of oxidation products was concentrated and acidified with sulfuric acid. There resulted 1.25 g of benzoic acid with m.p. 120° (57.4% of theoretical yield); identified by the mixing test with known acid. There was isolated from the filtrate by ether extraction 0.9 g of crude benzoylformic acid in the form of a dark oil, which crystallized upon storage desiccator. After pressing out on a plate, and crystallizing from water, the crystals melted at 56-57°. Literature data: m.p. 65° [20]. Yield – 0.4 g (30% of theoretical). With conc. H_2SO_4 it gave a characteristic violet color [18]. Due to insufficiency of material, the acid was characterized in the form of its phenylhydrazone [19]. The m.p. of the phenylhydrazone, 153°, corresponds to the literature data [19]. A sample mixed with the phenylhydrazone of the same acid, obtained according to Glücksmann [20], did not show depression.

Dealkylation of Ester (VII): α-Phenyl-β-bromhydrocinnamic acid (XII). 1.5 g of ester (VII) and 30 ml of glacial acetic acid saturated with HBr at 0° were placed in a thick-walled tube. The tube was sealed in the cold and was then heated at 80° for 12 hours in an oil bath with thermostat. The acetic acid was removed in vacuo after completion of the experiment. In the residue there was 0.95 g (69.1% of the theoretical quantity) of crude, yellow-colored acid (XII), which, after washing with ligroin and recrystallizing from chloroform-petroleum ether mixture (3:1), melted at 185° in conformity with the literature data [13]. For the comparison, known acid (XII) was obtained by the action of HBr in glacial acetic acid upon acid (X) which in its turn was synthesized according to directions given by the same author [13]. A mixed sample of the two specimens of acid (XII) melted without depression.

Found %: Br 26.07, 26.57. $C_{15}H_{13}O_2Br$. Calculated %: Br 26.18. Characteristic reaction: upon addition of an alcoholic solution of $AgNO_3$, AgBr precipitated, and from the filtrate, upon dilution, a flaky precipitate of stilbene separated (m.p. 124° [16].)

Synthesis of Ester (VII) from Known Acid (XII). 2 g of known acid (XII) and 50 ml of alcohol saturated with HCl were heated under reflux for 1 hour on a water bath. Concentration and subsequent cooling of the solution led to precipitation of colorless crystals of the ester (VII), with m.p. 129-130°. Yield – 2 g (93% of theoretical). After crystallization from alcohol, m.p. 131-132°. A sample mixed with ester (VII) obtained by condensation reaction melted at the same temperature.

IV. Condensation with Benzyl Bromide. 45 g of diazoacetate mixed with 40 g of benzyl bromide was added dropwise with stirring to 200 g of benzyl bromide and 0.5 g of copper powder, heated at 120°. 10.5 liters of nitrogen were evolved (21°, 768 mm). The reaction product was separated from catalyst by filtration and redistilled in vacuo. After distilling off the principal excess benzyl bromide (200 g, b.p. 82-85° at 14 mm), 8.2 g of a fraction with b.p. 93-96° at 14 mm was distilled off, which had an ethereal odor and was unsaturated with respect to $KMnO_4$. The content of this fraction was taken to be fumaric acid ester (according to the literature, b.p. is 98° at 14 mm) on the basis of having synthesized the diphenacylic ester, with m.p. 197.5°, from it by the earlier-described [2] method. The latter was identified with known diphenacylfumarate by the mixed sample test.

After removal of the fumarate, there remained in the distilling flask a viscous, resinous product of dark color, which was not distillable in a vacuum of 0.01 mm.

Investigation of the Non-Distillable Residue. The Hydrazide of Hydrocinnamic Acid. The ester of α-bromhydrocinnamic acid (XIII) was assumed to be present in the non-distillable residue, according to Equation (12). Because of the impossibility of separating the ester (XIII) from the residue, an attempt was made to convert it into cinnamic acid by the action of alcoholic alkali upon the entire resinous residue. Upon acidification of the alkaline solution, a viscous, dark-colored acid of semi-liquid consistency resulted, purification and characterization of which was unsuccessful. A second attempt consisted in a reductive dehalogenation of the residue [see Equation (13)].

20 g of zinc dust was gradually added to a mixture composed of 50 g of the resinous residue, 50 ml of 50% acetic acid, and 50 g of alcohol heated to 60°. After 1 hour of heating, the solution was separated from the zinc by filtration, the filtrate was diluted with water, and then neutralized with dry soda. The oily layer that separated was extracted with ether. After drying and distilling off the solvent, the oil was molecularly distilled in vacuo at 10^{-2} mm. It was possible to distill only a small portion of the product. Resulting fractions: I) b.p. 55-65°, n_D^{20} 1.4982-1.5000, 2.4 g; II) b.p. 65-75°, n_D^{20} 1.5056, 1 g; III) b.p. 85-95°, n_D^{20} 1.5240, 0.8 g; IV) b.p. 100-120°, n_D^{20} 1.5062. Results of the fractionation indicated the formation of quite a complex mixture of products. Only Fraction I was investigated, which was assumed to be the ethyl hydrocinnamate (XIV) on the basis of having derived from it the hydrazide (XV) with m.p. 99° according to the method of Jordan [21]. Because of insufficient amount of the substance, the hydrazide was purified by a single crystallization (from alcohol). The hydrazide of known hydrocinnamic acid (m.p. 48°) melted at 103° [21], and a mixed sample – at 100°.

SUMMARY

1. By condensing diazoacetate with di- and tri-phenylbrommethane in the presence of anhydrous copper sulfate, there can be obtained in one step, and with satisfactory yields, various compounds which are either not described in the literature, or which are not easily accessible for synthesis by other means.

2. Benzyl bromide in the presence of copper bronze also condenses with diazocetate, but only in negligible yield. The observed increase in yield of condensation product in the series benzyl bromide-diphenylbrommethane-triphenylbrommethane may be related to the decrease in energy of the C-Br bond in this series.

3. Various transformations of certain substances have been investigated for the purpose of determining their structures and for explaining the mechanism of reaction between halogen derivatives of the hydrocarbons with diazoacetate in the presence of copper catalysts.

4. The conclusion postulated regarding the mechanism of the reactions for all three halogen derivatives of the aliphatic-aromatic series investigated here allows one to assume a single common mechanism of interaction as for that described earlier for the halogen derivatives of the aliphatic hydrocarbons.

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* See Consultants Bureau translation, p. 953.

** See Consultants Bureau translation, p. 1393.

*** See Consultants Bureau translation, p. 63.

SULFONATION AND SULFONIC ACIDS OF ACIDOPHOBIC COMPOUNDS

XXI. SULFONATION OF 2,5-DIMETHYLTHIOPHENE. A COMPARISON OF THE SULFONATING ACTIONS OF PYRIDINE-SULFOTRIOXIDE, PYRIDINE-BIS-SULFOTRIOXIDE AND OF DIOXANE-SULFOTRIOXIDE

A. P. Terentyev and G. M. Kadatsky

In the works on sulfonation of various acidophobic compounds by one of us with his co-workers [1,2,3], various compounds of sulfuric anhydride were used: pyridine-sulfotrioxide ($Py \cdot SO_3$), pyridine-bis-sulfotrioxide ($Py \cdot S_2O_6$) and dioxane-sulfotrioxide ($D \cdot SO_3$). The actions of the first and second [1], and also of the first and third [2], were compared with thiophene and pyrrole derivatives. To compare their sulfonating actions on the same compounds, thiophene sulfonation was also carried out with $D \cdot SO_3$ and 2,5-dimethylthiophene with all three reagents.

On the basis of work carried out earlier on the sulfonation of pyrrole derivatives, it can be concluded that $D \cdot SO_3$ at room temperature and $Py \cdot SO_3$ at 100-120° possess the same sulfonating ability and give the same sulfoderivatives. It seemed that thiophene with $D \cdot SO_3$ should also produce the disulfoacids. However, the investigation carried out indicated that at room temperature thiophene is sulfonated to the monosulfo acid. Thus, $D \cdot SO_3$ is closer in its properties to $Py \cdot S_2O_6$ than the monosulfonating thiophene under the same conditions. With the use of two reagents, yields of the same order resulted – 75 and 86%, respectively.

A test of the action of three reagents on 2,5-dimethylthiophene has also indicated that $Py \cdot S_2O_6$ and $D \cdot SO_3$ react similarly, and give 2,5-dimethylthiophenylsulfonic-3-acid in almost theoretical yield – up to 95%. $Py \cdot SO_3$ even at 135° gives considerably lower yield of monosulfo acid (47%, calculated according to substance taken; 75% calculating on the basis of thioxene entered into reaction).

Interaction of $Py \cdot SO_3$ and thioxene showed a depressed activity for the latter as compared with thiophene, which under these conditions gave the disulfoacid in good yield. This result indicates: distinction between the α- and β-positions of the thiophene ring. Even when activated by methyl groups, the β-positions are considerably less reactive. This reaction also shows that 2,5-dimethylthiophene, with reference to its activity, is placed between thiophene and benzene, somewhat closer to the latter.

In one of the preceding articles [1], the possibility of direct synthesis of the sulfochloride from the pyridine salt which resulted from interaction of thiophene with $Py \cdot S_2O_6$ was demonstrated. In the present work, the 2,4-dimethylthiophenylsulfochloride synthesized by the same method, and without separating, was converted to the sulfamide with a total yield of 44 %.

In using $D \cdot SO_3$, the authors have taken approximately a double excess of dioxane in the sulfonation reaction. It is possible that the use of other ratios for dioxane and sulfuric anhydride will produce a sulfonating agent with somewhat different properties.

It is necessary to mention that the direct monosulfonation of 2,5-dimethylthiophene has been realized for the first time, by the authors. L. Keiser [4] obtained the monosulfo acid by an indirect method – by dehalogenation of 4-brom-2,5-dimethylthiophenylsulfonic-3-acid, obtained by the action of sulfuric acid on bromthioxene. W. Steinkopf, H. Jacob and H. Penz [5] obtained the anhydride of the disulfoacid in 50% yield by sulfonation of thioxene with 33% oleum.

EXPERIMENTAL

Thiophene was obtained by interacting sodium succinate with phosphorus pentasulfide [6]; 2,5-dimethylthiophene – by heating acetonylacetone; 2,5-dimethylfurane by hydrolysis with phosphorus trisulfide [7].

Sulfonation of 2,5-Dimethylthiophene

1. With Pyridinesulfotrioxide. 4 g of thioxene, 5.7 g of Py·SO_3 and 6 ml of dichlorethane were heated at 130° in a sealed tube to complete fusion of Py·SO_3 (8 hours). The cooled, light-brown sulfo mass was treated with water. The water layer was heated with an excess of barium carbonate for complete removal of pyridine and water vapor. After filtration, the aqueous solution was evaporated to a small volume and the salt was precipitated with alcohol; yield 4.55 g (46.6%). From the dichlorethane layer, by mercurization, was isolated 1.5 g of thioxene which did not enter into the reaction. The yield of salt, calculated on the basis of thioxene which entered into reaction, was 74.6%.

2. With Pyridine-bis-sulfotrioxide. 1.12 g of thioxene was added to Py·S_2O_6, prepared from 1.6 g of Py·SO_3 and 0.8 g of sulfuric anhydride in 8 ml of dichlorethane. After 24 hours the greenish reaction mass was treated with an excess of an aqueous suspension of barium carbonate, with heating. After the usual separation, 2.6 g (93.8%) of barium 2,5-dimethylthiophenylsulfonate-3 resulted.

3. With Dioxanesulfotrioxide. 3.36 g of thioxene was added to the D·SO_3 solution prepared from 4.8 g of sulfuric anhydride and 10 ml of dioxane in 48 ml of dichlorethane. After standing for 24 hours, the dark-colored reaction mass, from which at times dioxanesulfonate crystals precipitated, was treated as usual. 7.8 g (95.1%) of the barium salt resulted.

Barium 2,5-dimethylthiophenesulfonate – white lustrous scales, readily soluble in water.

3.068 mg substance: 1.321 mg $BaSO_4$. 7.792 mg substance: 3.345 mg $BaSO_4$. 3.390 mg substance: 1.481 mg $BaSO_4$. Found %: Ba 25.34, 25.26, 25.71. $C_{12}H_{14}O_6S_4Ba$. Calculated %: Ba 25.54.

The S-(α-naphthylmethyl)-thiouronic salt of 2,5-dimethylthiophenesulfonic-3 acid was obtained by the interaction of equivalent quantities of saturated aqueous solutions of naphthylmethylthiouronium chloride and the barium salt of thioxenesulfoacid. The resulting precipitate was recrystallized from aqueous alcohol, m.p. 195°.

4.840 mg substance: 0.304 ml N_2 (26°, 745 mm). Found %: N 6.80. $C_{18}H_{20}O_3N_2S_3$. Calculated %: N 6.87.

2,5-Dimethylthiophenesulfamide-3. To Py·S_2O_6, prepared from 4.8 g of Py·SO_3 and 2.4 g of sulfuric anhydride in 24 ml of dichlorethane, 3.36 g of thioxene was added. 6.3 g of phosphorus pentachloride was added after a period of 72 hours. After 3 hours the mixture was poured onto ice, and the dichlorethane layer separated. A concentrated solution of ammonia was added to it, the mixture concentrated on a water bath, and the residue reprocessed with ammonia and concentrated by evaporation.

The dry residue was placed in a glass tube, one end of which was pulled out to a capillary. This microflask extractor was suspended by a thin wire to a reflux condenser connected to a round-bottomed flask containing ether. The flask with the microextractor was placed in warm water and the sulfamide extracted by the ether flowing down from the condenser. The yield of amide was 2.2 g (44%), m.p. 141-142°. Literature data: m.p. 135° [4].

Sulfonation of Thiophene with Dioxanesulfotrioxide. 3 g of sulfuric anhydride dissolved in 30 ml of dichlorethane was added to 5 ml of dioxane with ice-water cooling and stirring, followed by 3.1 g of thiophene. After standing for three days and nights, the liquid, green in color, containing the dioxane salt crystals, was treated with water. 6.4 g of barium thiophenesulfonate-2 resulted from the aqueous solution by the usual procedure. Yield was about 75% calculated on the basis of thiophene taken.

SUMMARY

A comparison of the sulfonating actions of pyridinesulfotrioxide, pyridine-bisulfotrioxide and dioxanesulfotrioxide, with the examples of thiophene and 2,5-dimethylthiophene sulfonation, have been carried out in this work. It has been demonstrated that the last two reagents are similar in action. They sulfonate thiophene with 86 and 75% yields, and 2,5-dimethylthiophene with 94 and 95%, respectively, producing the monosulfo derivatives. Pyridinesulfotrioxide at 130° also gives the monosulfo acid of 2,5-dimethylthiophene, but with 75% yield, calculated on the basis of thioxene that entered into reaction.

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THE SULFONATION REACTION

XXVI. DETERMINATION OF SOME DI- AND TRI-SULFOACIDS OF NAPHTHALENE

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The authors at an earlier date [1] developed a method for the quantitative determination of 1,5-, 2,6- and 2,7-disulfoacids of naphthalene in sulfonation mixtures which do not contain the monosulfoacids of naphthalene. A brief review of the literature on analysis of disulfo mixtures was given in the work mentioned. The foundation of the present work on analysis of naphthalene disulfoacids is the method of exhaustive sulfonation. This method was proposed for the first time by V. N. Ufimtsev and A. F. Krivoshlykova [2] who, after sulfonation with oleum, nitrated the mixture and then reduced the nitrogroups, and diazotized the aminosulfoacid. Thus, the relative quantities of 1,6- and 1,7-naphthalenedisulfoacids were determined, but the method was not tested on artificial mixtures in the presence of other isomers, and the degree of its accuracy is apparently not high. Lantz [3] likewise used essentially the same method, after sulfonation, nitrating the mixture in the cold and with heating. However, this method was tested by Lantz without the presence of 1 7- and 13-isomers, and requires large corrections which are experimentally found for each determination, which makes it unreliable.

Upon exhaustive sulfonation with oleum, 1,5-, 1,7- and 2,6-naphthalenedisulfo-acids convert into 1,3,5,7-tetrasulfoacid, and the 1,6- and 2,7-disulfoacids into 1,3,6-trisulfoacid. As shown below, the 1,3-disulfo acid sulfonates to the extent of 75% into 1,3,5,7-tetrasulfoacid.

In addition to the exhaustive sulfonation, as a basis of the method is observation that 1,3,5,7-naphthalenetetrasulfochloride is almost completely insoluble in benzene, while 1,3,6-naphthalenetrisulfochloride dissolves in the amount of 10.7 g per 100 g of solution [4]. Therefore, the disulfoacid mixture is sulfonated with oleum, and then chlorsulfonic acid is added to the mixture to convert the sulfo acids into the chlorides. The mixture is poured onto ice, the chlorides are filtered off, dried, weighed, and then treated on the filter with benzene. After weighing the tetrachloride residue, the ratio of disulfoacids sulfonating to tri- and tetra-derivatives is determined.

In combination with the earlier developed method [1] for the determination of 1,5-, 2,7- and 2,6-isomers, the exhaustive sulfonation method permits determination of the 1,6-isomer, and by difference the 1,7-isomer, also, in the absence of 1,3-disulfoacid in the mixture. With a small amount of the latter, its sum with the 1,7- isomer is determined with some error.

The method described above also permits determination of the 1,3,6-trisulfoacid and the sum total of 1,3,5- and 1,3,7-trisulfoacids in a mixture containing trisulfoacids of naphthalene.

EXPERIMENTAL

The tri- and tetra-sulfoacids are not completely converted into the chlorides by the action of chlorsulfonic acid; therefore, the first prerequisite is to demonstrate that tri- and tetra-chlorides are formed in the same ratios in which the tri- and tetra-sulfoacids are present in the mixture at the start.

A weighed portion of 1,3,6-naphthalenetrisulfochloride, m.p. 198.5°, was mixed with a weighed portion of 1,3,5,7-tetrachloride, m.p. 272°. The chlorides were dissolved in mixtures of variable composition of chlorsulfonic and sulfuric acids, the solution was heated for 2 hours at 125°, and then was poured on ice. The chlorides were filtered off, washed, dried and weighed. The 1,3,6-trichloride was then washed with benzene on the filter, and from the tetrachloride residue the ratio with chlorides was determined. The experimental results, given in Table 1, indicate that the sulfoacids convert into the chlorides, and in the same ratios in which they are present dissolved in a mixture of chlorsulfonic and sulfuric acids.

TABLE 1

Isolation of the Chlorides from a Solution Containing a Mixture of Chlorsulfonic and Sulfuric Acids.

Expt. No.	Taken (in %)		Found (in %)	
	1,3,6-tri-chloride	1,3,5,7-tetra-chloride	tri-chloride	tetra-chloride
219	10.6	89.4	11.1	88.9
226	50.5	49.5	51.2	48.8
225	58.5	41.5	59.0	41.0
224	81.0	19.0	81.6	18.4

The procedure was then developed for sulfonation experiments on disulfochloride mixtures. A weighed portion of the pure disulfochlorides was placed in a test tube and 3 ml of 55-65% oleum was added, about 1 g in total weight. The test tube was sealed and heated at a temperature of 160-162° for 2-3 hours. The tube was then opened and 5 ml of chlorsulfonic acid was added and the mixture again heated at 120-125° for 2 hours to convert the sulfoacids into the chlorides. The mixture was then poured onto ice, the chlorides filtered off, washed with water, dried, weighed, washed with benzene, and the residue again weighed.

The experimental results given in Table 2 indicate that the deviation after conversion of the tetrachloride to the dichloride does not exceed 1%. At the same time, the 1,3-disulfochloride forms 75% of the tetrasulfoacid and 25% of the trisulfoacid. The tetrachloride was obtained with somewhat lower melting point than the pure product (Table 2).

TABLE 2
Exhaustive Sulfonation of Naphthalenedisulfochloride at a Temperature of 160-162°

Experiment No.	Dichloride taken (in % of the total weighed portion)						Tetrachloride found by conversion to dichloride (%)	Difference (in %)	Melting point of the tetrachloride
	1,3-	1,5-	1,6-	1,7-	2,6-	2,7-			
252	100						76.8		252°
246	100						74.5		249
251			51.7	48.3			51.2	0.5	250
228					30.6	69.4	29.8	0.8	252
233					94.2	5.8	94.2	0	261
245		9.6	90.4				9.2	0.4	
248		10.1	89.9				10.2	0.1	
204		29.4	70.6				28.4	1.0	255
239		31.3	68.7				31.1	0.2	
205		44.6	55.4				44.8	0.2	252
247		50.2	49.8				51.0	0.8	
250		78.7	21.3				77.9	0.8	254
236		79.3	20.7				78.6	0.7	258
214		93.4	6.6				93.7	0.3	254

Finally, the method was tested on artificial mixtures of the pure disulfoacids of naphthalene. To a weighed portion of about 1 g of the disulfoacid mixture, containing a known quantity of water of hydration, 2 to 2.3 g of the monohydrate of sulfuric acid was added. The mixture thus resulted in an H_2SO_4 concentration of 86-90%, approximating that resulting from sulfonation of naphthalene to the disulfo stage with the monohydrate of 98% H_2SO_4. 5-7 ml of oleum was added to the mixture and the sulfo mass was heated for 2 hours at 160° in a sealed test tube. The sulfo acids were then converted to the chlorides by heating with 15 ml of chlorsulfonic acid. Further steps are described above. The experimental results given in Table 3 indicate that with the sulfo acid mixture the determination errors again usually do not exceed 1%.

Determination. About 3 g of the sulfo mass (weighed on technical scales) with a content of about 1 g of disulfoacids is placed in a test tube and 7 ml of 65% oleum added. The test tube is sealed and placed in a safety iron tube with screw top through a socket in which is passed a thermometer and the tube is placed in an Eijkman apparatus. After heating at 161-163° for 2 hours with boiling butyric acid in the outer container of the Eijkman apparatus, the test tube is unsealed, 15 ml of chlorsulfonic acid added to the sulfo mass, and the mixture heated to 120-125° for one hour. The mass is then poured onto pure ice; the chlorides which result in the amount of about 0.5-0.6 g are filtered off, washed with water, dried, weighed, washed about six times with benzene, taking 5 ml portions for each washing, and the residue then weighed again. 2-3 drops of the filtrate from the last washing with benzene is evaporated on a watch glass. If a residue is not evident, then the washing is terminated. Before pouring the mass onto ice it is necessary to see that tetrachloride precipitate not separate from the reaction mixture. This distorts the results. In such case the mixture is heated anew to the dissolution of the precipitate, and, if necessary, chlorsulfonic acid is added and the mixture then poured while warm onto the ice.

The % of disulfoacids sulfonating to the tetrasulfoacid is determined by the formula:

$$\%\,(1{,}5\text{-},\ 1{,}7\text{-},\ 2{,}6\text{-acid}) = \frac{430}{5.3\,\frac{a}{b} - 1},$$

TABLE 3
Exhaustive Sulfonation of Naphthalenedisulfoacids at 160° for 2 hours.

Experiment No.	Disulfoacids taken (in % of total weighed batch)						Oleum taken (in ml)	Tetrachloride found by conversion to disulfoacid (%)	Difference (in %)	Melting point of the tetrachloride
	1,3-	1,5-	1,6-	1,7-	2,6-	2,7-				
256		63.3	36.7				5	63.2	0.1	250°
257		58.2	41.8				5	58.5	0.3	258
273					27.8	72.2	6	27.4	0.4	
275			21.8	9.8	26.4	42.0	7	35.5	0.7	250
276			17.3	14.3	24.2	44.2	7	39.0	0.5	245
264		48.7	23.5	10.0	–	17.8	6	58.1	0.6	255
268		58.7	20.7	11.0	–	9.6	6	69.6	0.1	259
259	17.5	41.2	23.7	10.5	–	7.1	6	65.0	0.2 •	249
265	16.3	40.5	23.9	9.4	–	9.9	6	61.6	0.5 •	257

• It is considered that 1,3-disulfoacid converts to the extent of 75% into tetrasulfoacid and 25% into trisulfoacid.

where a = weight of tri- and tetra-chloride mixture, b = weight of tetrachloride.

Together with the earlier-described [1] method for determination of 1,5-, 2,6-, and 2,7-disulfoacids, the present method permits a complete analysis of the disulfomixtures resulting at low temperature, in the absence of 1,3- and 2,6-disulfoacids. These methods applied to disulfomixtures obtained at a temperature of about 130° cannot give accurate results since in such a mixture a considerable quantity of 1,3-disulfoacid will be present, which does not sulfonate completely to the tetrasulfoacid. Both methods are applicable to sulfo mixtures obtained at high temperatures (150-180°), since with a complete absence of the 1,5-disulfoacid the mixture is composed primarily of 2,6- and 2,7-isomers, and the 1,3-acid content in the presence of 1,6- and 1,7-isomers is also negligible. In such mixtures it is possible to determine 2,6-, 2,7- and 1,6- and the sum of 1,7- and 1,3-isomers. This method is also applicable, with equal success, to an analysis of naphthalene trisulfoacid mixtures. At the same time the content of 1,3,6-trisulfoacid and the sum of 1,3,5- and 1,3,7-trisulfoacids can be determined.

The following products were used by the authors in their work: 1,5-naphthalenedisulfochloride, m.p. 184°; 1,3-dichloride, m.p. 137°; 1,7-dichloride, m.p. 122°; 1,6-dichloride, m.p. 129°; 2,6-dichloride, m.p. 226°, and 2,7-dichloride with an m.p. of 162°. Free disulfoacids resulted in which the content of water of crystallization was determined alkalimetrically by saponification of the chlorides with water-alcohol mixture, and the solution evaporated to dryness on a water bath. Distilled chlorsulfonic acid and pure oleum were used.

SUMMARY

A method for the quantitative determination of two naphthalenedisulfoacid groups (sulfonating to the tetrasulfoacid and to the trisulfoacid) has been developed by the method of exhaustive sulfonation, conversion of the polysulfoacids into the chloranhydrides, and separation of the latter by treatment with benzene.

The method is applicable to the analysis of naphthalenesulfoacid mixtures. The error in determination of the isomers does not exceed 1% by the method described.

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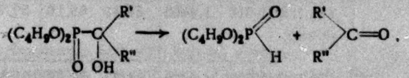
• See Consultants Bureau English translation page 1663.
•• See Consultants Bureau English translation page 2091.

INTERACTION OF DIALKYLPHOSPHOROUS ACIDS WITH ALDEHYDES AND KETONES

IV. BUTYL AND ALLYL ESTERS OF α-HYDROXYALKYLPHOSPHINIC ACIDS

V. S. Abramov, R. V. Dmitrieva and A. S. Kapustina

The butyl and allyl esters of various α-hydroxyalkylphosphinic acids are described in the present article. The esters were obtained by methods described in the preceding articles [1] by the authors – by reacting dibutylphosphorous and diallylphosphorous acids with various aldehydes and ketones in the presence of freshly-prepared sodium methylate. The reaction proceeds rapidly. The reaction products can be immediately fractionally distilled. Upon interaction of dibutylphosphorous acid with methylpropylketone, diethylketone and with dibenzylketone, there is a temperature rise of from 16° to 27°. Such a rise in temperature undoubtedly indicates progress in the reaction and formation of the butyl esters of the corresponding α-hydroxyalkylphosphinic acids. However, upon fractionally distilling the reaction products, it appeared impossible to separate the butyl ester of α-hydroxyalkylphosphinic acid. During fractional distillation dibutylphosphorous acid distilled off slowly. More rapid and intense heating during the fractional distillation led to violent decomposition. The authors consider that during the fractional distillation, there occurs a gradual decomposition of the butyl ester of α-hydroxyalkylphosphinic acid:



Dibutylphosphorous acid distills off as it forms. The ketones present – methylpropylketone and diethylketone – are removed in vacuo without condensation, dibenzylketone being recovered completely from the reaction.

Upon interacting dibutylphosphorous acid with isovaleric aldehyde, the reaction mass temperature rose from 20° to 104° and the butyl ester of α-hydroxy-γ-methylbutylphosphinic acid was no doubt formed. The ester was isolated, but upon its fractional distillation, partial decomposition occurred. The acid formed was added to the ester and increased the phosphorous content. From the resulting partial decomposition may be explained the high phosphorous content as compared with theory.

Upon interacting diallylphosphorous acid with isovaleric and with benzoic aldehydes, the temperature of the reaction mass rose with reaction from 23° to 45°, and with the benzoic, from 20° to 98°. Allyl ester of α-hydroxyalkylphosphinic acids were formed. However, esters were not obtained in the pure state since gradual decomposition occurred during their fractional distillation. It was even possible to partially redistill the allyl ester of α-hydroxybenzylphosphinic acid, but at the same time it contained a large quantity of decomposition products. The residue polymerized to a hard mass with violent decomposition. A similar picture resulted from the interaction of diallylphosphorous acid with methylethylketone and acetophenone. From the heat evolved during the course of the reaction, it should be considered that the allyl esters of the corresponding α-hydroxyalkylphosphinic acids are produced; however, they failed to separate.

An interesting case is that of interaction between dibutylphosphorous acid and the ethyl ester of 2-ketocyclopentanecarboxylic acid. If dibutylphosphorous acid reacts vigorously with cyclopentanone and with cyclohexanone with large heat evolution and with formation of the butyl esters of α-hydroxycyclopentylphosphinic and α-hydroxycyclohexylphosphinic acids, then the presence of a carbon atom of the carbethoxyl group adjacent to the carbonyl group eliminates the reaction. Here the effect of the carbethoxyl group is evident.

EXPERIMENTAL

The experiments were carried out in the same manner as described in the preceding articles, a few drops of freshly-prepared sodium methylate being added to an equimolecular mixture of the dibutylphosphorous or diallylphosphorous acid and the aldehyde or the ketone. After standing, or upon heating in some cases, the reaction products were fractionally distilled in vacuo. Data for the resulting butyl and allyl esters of the various α-hydroxyalkylphosphinic acids are given in Tables 1 and 2.

TABLE 1

n-Butyl Esters of α-Hydroxyalkylphosphinic Acids

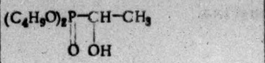
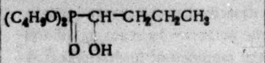
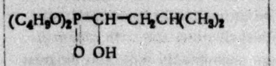
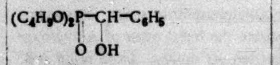
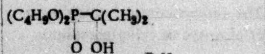
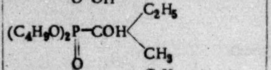
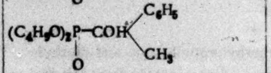
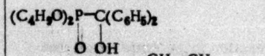
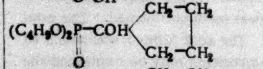
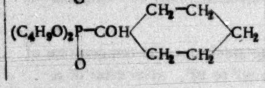
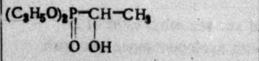
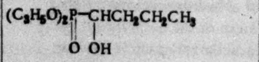
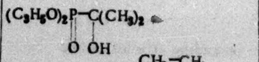
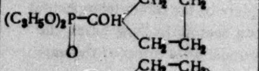
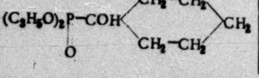
No.	Formula for the ester obtained	Boiling point	d_4^{20}	n_D^{20}	MR_D Calculated	MR_D Found	Ester yield (%)	Phosphorous content (in %) Calculated	Phosphorous content (in %) Found
1	 $(C_4H_9O)_2P(=O)-CH(OH)-CH_3$	162-163° (9 mm)	1.024	1.4384	60.26	61.08	56.7	13.03	13.25; 13.35
2	 $(C_4H_9O)_2P(=O)-CH(OH)-CH_2CH_2CH_3$	168-170° (6 mm)	1.000	1.4400	69.49	70.06	49.0	11.65	11.90; 11.84
3	 $(C_4H_9O)_2P(=O)-CH(OH)-CH_2CH(CH_3)_2$	180-182° (11 mm)	0.998	1.4360	74.11	73.42	–	11.07	14.08; 14.20
4	 $(C_4H_9O)_2P(=O)-CH(OH)-C_6H_5$	168-170° (5 mm)	1.026	1.4680	79.75	81.28	–	10.33	10.02; 10.87
5	 $(C_4H_9O)_2P(=O)-C(OH)(CH_3)_2$	154-155° (7 mm)	1.018	1.4366	64.88	64.81	59.2	12.30	12.53; 12.34
6	 $(C_4H_9O)_2P(=O)-COH(C_2H_5)(CH_3)$	156-157° (8 mm)	1.015	1.4403	69.49	69.16	57.7	11.65	11.53; 11.72
7	 $(C_4H_9O)_2P(=O)-COH(C_6H_5)(CH_3)$	179-180° (9 mm)	1.025	1.4670	84.37	84.99	30.0	9.87	10.05; 10.07
8	 $(C_4H_9O)_2P(=O)-C(OH)(C_6H_5)_2$	207-209° (7 mm)	1.030	1.4760	103.85	102.93	–	8.24	9.17; 9.03
9		179-180° (9 mm)	1.049	1.4549	71.92	71.87	40.4	11.15	11.34; 11.22
10		178-180° (7 mm)	1.039	1.4570	76.53	76.53	48.7	10.62	10.91; 10.98

TABLE 2

Allyl Esters of α-Hydroxyalkylphosphinic Acids

No.	Formula for the ester obtained	Boiling point	d_4^{20}	n_D^{20}	MR_D Calculated	MR_D Found	Ester yield (%)	Phosphorous content (in %) Calculated	Phosphorous content (in %) Found
1	 $(C_3H_5O)_2P(=O)-CH(OH)-CH_3$	151° (10 mm)	1.1187	1.4565	49.99	50.09	65.3	15.05	14.53; 14.92
2	 $(C_3H_5O)_2P(=O)-CH(OH)CH_2CH_2CH_3$	163-164° (10 mm)	1.0769	1.4552	59.33	58.98	31.6	13.25	13.22; 13.28
3	 $(C_3H_5O)_2P(=O)-C(OH)(CH_3)_2$	132° (12 mm)	1.0907	1.4500	50.03	50.24	38.8	14.06	14.08; 14.19
4		165-167° (7 mm)	1.1253	1.4740	61.74	61.47	45.7	12.60	11.94; 11.97
5		m.p. 56.5-57°	–	–	–	–	67.7	11.92	12.03; 11.90

Interaction of Dibutylphosphorous Acid with Methylpropylketone, Diethylketone and Dibenzylketone. 9.7 g (0.05 mole) of dibutylphosphorous acid and equimolecular quantities of the following were taken for reaction, respectively: 4.3 g of methylpropylketone, 4.3 g of diethylketone and 9.1 g of dibenzylketone. A few drops of freshly-prepared sodium methylate was added to each mixture. The reaction mass temperature upon addition of the sodium methylate increased from 20° to 37° in the reaction of dibutylphosphorous acid with methylpropylketone, from 17° to 33° in the reaction with diethylketone, and from 21° to 48° in the reaction with dibenzylketone.

The reaction products were heated on a paraffin bath at 120° to 130° for a prolonged period of time. Upon fractional distillation the initial substances in all cases were recovered with small losses.

Interaction of Dibutylphosphorous Acid with the Ethyl Ester of 2-Ketocyclopentanecarboxylic Acid. 9.7 g of dibutylphosphorous acid and 7.8 g of the ethyl ester of 2-ketocyclopentanecarboxylic acid were taken for reaction. The temperature of the reaction mass rose from 20° to 23° upon addition of the sodium methylate. The reaction mass was heated on a paraffin bath at 140-150° for a prolonged period. During fractional distillation in vacuo, the fractions obtained were: 3.6 g of the ethyl ester of 2-ketocyclopentanecarboxylic acid and 4 g of dibutylphosphorous acid. The residue – a non-distillable resinous mass.

Interaction of Diallylphosphorous Acid with Isovaleric Aldehyde. 8.1 g of diallylphosphorous acid and 4.5 g of isovaleric aldehyde were taken for reaction. The temperature of the reaction mass rose from 23° to 45° upon addition of freshly-prepared sodium methylate to the mixture. During fractional distillation of the reaction product, the initial substances were distilled off. The allyl ester of α-hydroxy-γ-methylbutylphosphinic acid was not obtained.

Interaction of Diallylphosphorous Acid with Benzoic Aldehyde. 8.1 g of diallylphosphorous acid and 5.3 g of benzaldehyde were taken for reaction. Several drops of freshly-prepared sodium methylate was added to the mixture. The temperature of the reaction mass rose from 20° to 98°. The product was then fractionally distilled in vacuo. Fractionation was carried out at 8 mm of final pressure with partial decomposition. At 170° violent decomposition occurred with formation of a light, foamy, hard product. During repeated distillations of the product which distilled during the first fractionation, up to 170°, violent decomposition was again repeated with the same picture of hard foam formation. The allyl ester of α-hydroxybenzylphosphinic acid did not result.

Interaction of Diallylphosphorous Acid with Methylethyl ketone and with Acetophenone. 8.1 g of diallylphosphorous acid and 4 g of methylethyl ketone or 6 g of acetophenone, were taken for reaction. Upon addition of sodium methylate to the reaction mass, the reaction temperature rose from 23° to 44° in the reaction with methylethyl ketone, and in the reaction with acetophenone – from 23° to 62°. The allyl esters of the corresponding α-hydroxyalkylphosphinic acids did not result upon fractional distillation of the reaction products. The initial products were recovered.

SUMMARY

1. Dibutylphosphorous acid and diallylphosphorous acid in the presence of sodium methylate reacts with aldehydes and ketones to give esters of α-hydroxyalkylphosphinic acids. Ten butyl esters of various α-hydroxyalkylphosphinic acids and five allyl esters of various α-hydroxyalkylphosphinic acids have been obtained.

2. Dibutylphosphorous acid and diallylphosphorous acid react with a whole series of other aldehydes and ketones; however, the esters of the corresponding α-hydroxyalkylphosphinic acids fail to separate. Upon fractional distillation decomposition to the original substances takes place. The decomposition process proceeds more rapidly the greater the radical size of the dialkylphosphorous acid.

LITERATURE CITED

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* See Consultants Bureau English translation, page 701.

THE SYNTHESIS AND PROPERTIES OF VINYLPHOSPHINIC ESTERS

I. THE PHOSPHONETHYLATION REACTION. ADDITION OF DIALKYLPHOSPHOROUS ACIDS, AMMONIA AND AMINES TO THE ETHYL ESTER OF VINYLPHOSPHINIC ACID.

A. N. Pudovik and G. M. Denisova

In a series of works completed by one of us and published in this journal over the past two years, a new method for the synthesis of various ester derivatives of phosphinic acids was developed, which consists of adding dialkylphosphorous acids to unsaturated electrophilic reagents: unsaturated ketones, aldehydes, nitriles, acids and their esters, and esters of the vinyl alcohols [1]. With the help of this method, a number of unknown esters of ketophosphinic, hydroxyphosphinic and cyanphosphinic acids, as well as esters of the phosophocarboxylic acids, and others, have been synthesized. As has already been mentioned, it is a very simple method in procedure, the initial components are readily accessible, and in a majority of the cases leads to the formation of phosphinic acid esters in good yield.

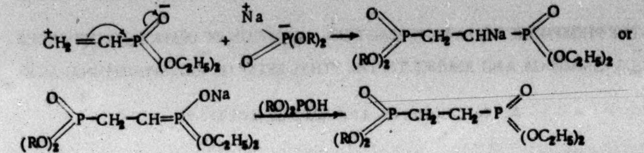
To develop and to expand this investigation, the authors have decided in the present work to investigate the possibility of using addition reactions between an electrophilic reagent and esters of vinylphosphinic acid. Esters of vinylphosphinic acid and the homologs have not been used up to the present time for addition reactions, and it should be mentioned in general that this interesting group of organophosphorous compounds has as yet received but little study. The literature contains a description for the satisfactory synthesis of only the simplest representative of the unsaturated phosphinic ester series — namely, that of the ethyl ester of vinylphosphinic acid [2], which has also been used by the authors. The vinylphosphinates have been found to be readily obtainable, and, which is equally important, they are adequately stable, do not polymerize upon prolonged storage at room temperature or during the process of vacuum fractional distillation, or when heated for several hours on a water bath.

The first experiments carried out with vinylphosphinates indicated that they are sufficiently reactive to allow dialkylphosphorous acids to add to them in the presence of alcoholates of alkali metals. Since the reaction of addition to unsaturated phosphinates has received no study at all up to the present time, it was of interest therefore, to attempt their addition to other nucleophilic reagents usually used for similar purposes, in addition to the dialkylphosphorous acids. Preliminary experiments carried out along these lines have shown that ammonia, amines, malonic, cyanacetic and acetoacetic esters and their homologs, and also certain other reagents with mobile hydrogen atoms, add easily and rapidly to vinylphosphinate in the presence of alkali metal alcoholates, and in some cases without. Thus, this new reaction of nucleophilic reagent addition to vinylphosphinate which has been discovered by the authors, apart from its theoretical interest, may also prove to be of practical import for the synthesis of various phosphinate derivatives.

For convenience, and in order to reflect the basic nature of the process, it has been considered expedient to call this reaction which the authors have newly discovered "the phosphonethylation reaction", by analogy with the known and now widely-used cyanethylation reaction, by the use of which phosphonethylation reaction the phosphonethyl group can be introduced into various organic compounds. In the present article the authors have described addition to vinylphosphinate of dialkylphosphorous acids, of ammonia, and of some amines, for the most part secondary.

Addition of dialkylphosphorous acids to vinylphosphinate was carried out by the authors in the presence of alkali metal alcoholates. To avoid exchange of radicals between the alcoholates and the dialkylphosphorous acids, alcoholates with the same radicals as were contained in the dialkylphosphorous acids being added were used in the reactions. Reaction proceeded rapidly and was accompanied by strong heat evolution from the reaction mixtures. Yields of the addition products for the lower dialkylphosphorous acids constituted about 60% of the theoretical. The resulting esters of di-(dialkylphosphon)-ethane were viscous, colorless liquids, readily soluble in water, combining with alcohol and with ether in all proportions. The product obtained by addition of diethylphosphorous acid to vinylphosphinate was found to be identical with 1,2-di-(diethylphosphon)-ethane synthesized according to Ford-Moore [3] by reaction of triethylphosphite with ethylene bromide. Constants for the latter product are: b.p. 167° (1 mm); $n_D^{16.5}$ 1.4425; as obtained by the authors from the addition reaction, 1,2-di-(diethylphosphon)-ethane had a b.p. of 164-165° (2 mm); n_D^{20} 1.4410; d_4^{20} 1.1376. The mechanism of the addition reaction may be expressed by the following general scheme:

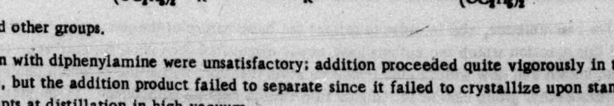
$$(RO)_2POH + RONa \rightleftharpoons (RO)_2PONa + ROH.$$



The authors proceeded to investigate addition reactions of ammonia and amines to vinylphosphinate. The first experiments which involved the addition of ammonia to vinylphosphinate were carried out in aqueous and in alcoholic solutions at room temperature, without catalyst, and did not lead to positive results. Only by conducting the reaction in alcoholic solution, and in the presence of a small quantity of methyl alcoholate, did the reaction proceed successfully, leading to a 67.3% yield of β-diethylphosphonethylamine; b.p. 93-95° (4 mm); n_D^{20} 1.4270; d_4^{20} 1.0515. The ethylaminophosphinic acid itself was earlier synthesized by rather complex methods; by Finkelstein — from the ethyl ester of β-diethylphosphonpropionic acid [4], and by Kosollapoff [5] — by interaction of β-bromethylphthalimide and triethylphosphite with subsequent saponification of the reaction product. Incidentally, it should be mentioned that with few exceptions very little is known at present about the aminophosphinates and their derivatives. Recently, M.I. Kabachnik and his co-workers [6] obtained aminomethylphosphinic acid and some of its derivatives, utilizing the reaction between the ester of chlormethylphosphinic acid and ammonia.

With further investigation of the addition reaction of secondary amines to vinylphosphinate, there was observed the exceptional ease with which the lower aliphatic secondary amines added. The addition of dimethylamine to vinylphosphinate occurred immediately upon combining with one another, while at the same time the reaction mixture temperature rose to +55°. After standing for 24 hours at room temperature, the yield of addition product — β-diethylphosphonethyldimethylamine — constituted 83%. The β-diethylphosphonethyldimethylamine was confirmed by its synthesis from β-bromethylphosphinic ester and dimethylamine. The constants for the two products were found to be identical. The addition of piperidine to the vinylphosphinic ester proceeded somewhat less vigorously. After combining the reagents, the temperature of the reaction mixture had risen to 40°, 20 minutes after start of the experiment. Reaction proceeded without the need for any special catalyst, and after 24 hours standing at room temperature, the reaction product was obtained in a yield of 52.6%. The addition of aniline to the vinylphosphinic ester was attainable only in the presence of catalyst — sodium methylate; and the reaction did not go very smoothly. Along with the addition product — β-diethylphosphonethylaniline, which resulted only in negligible yield — a large quantity of low-boiling fraction was obtained.

The addition of amines to the vinylphosphinic ester may be represented by the following scheme:



where R = H, CH_3, C_6H_5, and other groups.

Results of reaction with diphenylamine were unsatisfactory; addition proceeded quite vigorously in the presence of sodium ethylate, but the addition product failed to separate since it failed to crystallize upon standing, and decomposed with attempts at distillation in high vacuum.

EXPERIMENTAL

Addition of Dimethylphosphorous Acid to Vinylphosphinic Ester. Saturated sodium methylate solution in methyl alcohol was added dropwise to the reaction mixture, which consisted of 8.2 g of vinylphosphinic ester and 5.5 g of dimethylphosphorous acid. The reaction proceeded very violently with strong heat evolution, and even with boiling of the reaction mixture; during the process of reaction, considerable increase in viscosity was observed. After standing for 24 hours at room temperature the reaction mixture was fractionally distilled in vacuo from a small Arbuzov flask. From the fractional distillation there resulted a small quantity of initial dimethylphosphorous acid and 7.2 g of 1-dimethylphosphon-2-diethylphosphonethane;

b.p. 158-160° (2 mm); n_D^{20} 1.4430; d_4^{20} 1.2075; MR_D 60.82; calculated 60.87.

0.1460 g substance: 67.7 ml NaOH (T = 0.017841). Found %: P 23.1. $C_8H_{20}O_6P_2$.
Calculated %: P 23.4.

Addition of Diethylphosphorous Acid to Vinylphosphinic Ester. A saturated solution of sodium ethylate in ethyl alcohol was added dropwise to the reaction mixture which consisted of 6 g of vinylphosphinic ester and 5 g of diethylphosphorous acid. The reaction proceeded as vigorously as in the preceding experiment. From fractional distillation of the reaction mixture, there resulted 6.3 g of 1,2-di(diethylphosphone)ethane;

b.p. 164-165° (2 mm); n_D^{20} 1.4410; d_4^{20} 1.1376; MR_D 70.13; calculated 70.10.

0.1614, 0.1526 g substance: 6.6, 6.35 ml NaOH (T = 0.017841). Found %: P 20.2, 20.5.
$C_{10}H_{24}O_6P_2$. Calculated %: P 20.5

Addition of Dibutylphosphorous Acid to Vinylphosphinic Ester. Reaction was carried out with 4.6 g of vinylphosphinic ester and 5.5 g of dibutylphosphorous acid in the presence of sodium butylate. From the first fractional distillation of the reaction mixture, 5.2 g of 1-diethylphosphon-2-dibutylphosphonethane resulted;

b.p. 197-199° (2 mm); n_D^{20} 1.4430; d_4^{20} 1.0681; MR_D 88.6; calculated 88.1

0.1435 g substance: 49.8 ml NaOH (T = 0.017841). Found %: P 17.1. $C_{14}H_{32}O_6P_2$.
Calculated %: P 17.3

Addition of Ammonia to Vinylphosphinic Ester. Experiment I. 10.4 g of the vinylphosphinic ester was added to 65 g of concentrated aqueous ammonia. The mixture was left standing at room temperature for 24 hours. After distilling off the ammonia and water in low vacuum, the residue was a hard glassy mass.

Experiment II. 7 g of vinylphosphinic ester was added to 54.5 g of ethyl alcohol containing 10 g of ammonia. After standing for 24 hours at room temperature in a covered flask, followed by subsequent fractional distillation, the initial products were recovered (with the exception of a small fraction boiling in the range of 95-100° at 5 mm).

Experiment III. The experiment was carried out identically with the preceding, using 15 g of vinylphosphinic ester in the presence of sodium methylate. There resulted, upon fractional distillation of the reaction mixture, 11 g of the ethyl ester of β-diethylphosphonethylamine;

b.p. 93-95° (4 mm); n_D^{20} 1.4270; d_4^{20} 1.0515; MR_D 44.20; calculated 44.19.

0.1486 g substance: 47.4 ml NaOH (T = 0.017841). Found %: P 16.6. $C_6H_{16}O_3NP$.
Calculated %: P 17.0.

Addition of Dimethylamine to Vinylphosphinic Ester. 4.5 g of dimethylamine was added to 5 g of vinylphosphinic ester. Heat evolution from the reaction mixture was observed up to 55°. The mixture was left standing at room temperature for 24 hours, after which it was fractionally distilled in vacuo. 5.3 g of β-diethylphosphonethyldimethylamine resulted;

b.p. 103-104° (4 mm); n_D^{20} 1.4345; d_4^{20} 1.0157; MR_D 53.6; calculated 53.9.

0.1455 g substance: 44.2 ml NaOH (T = 0.017841). Found %: P 14.9. $C_8H_{20}O_3NP$. Calculated %: P 14.8.

Action of Dimethylamine Upon Ethyl β-Bromethylphosphinic ester. A mixture of 10 g of β-bromethylphosphinic ester, 7.5 g of dimethylamine and 25 ml of water was left standing for 2 hours. 25 ml of 20% caustic soda solution was then added to it. The reaction mixture was then extracted with 100 ml of benzene, the benzene solution dried with calcium chloride, the benzene distilled off on a water bath, and the residue distilled in vacuo. 3.2 g of β-diethylphosphonethyldimethylamine resulted;

b.p. 108-109° (6 mm); n_D^{20} 1.4340; d_4^{20} 1.0154.

Addition of Piperidine to Vinylphosphinic Ester. 3.7 g of piperidine was added to 5 g of vinylphosphinic ester. Little heat evolution from the reaction mixture was observed. It was left standing at room temperature for 24 hours and was then fractionated. 4 g of β-diethylphosphonethylpiperidine was separated:

b.p. 135-137° (3 mm); d_4^{20} 1.0514; n_D^{20} 1.4605; MR_D 64.82; calculated 65.5.

0.128 g substance: 32.9 ml NaOH (T = 0.017841). Found %: P 12.6. $C_{11}H_{24}O_3NP$. Calculated %: P 12.5.

An analogous product resulted from β-bromethylphosphinate and piperidine.

Addition of Aniline to Vinylphosphinic Ester. Sodium methylate solution was added dropwise to a mixture of 7 g of vinylphosphinic ester and 4 g of aniline. Temperature of the reaction mixture rose rapidly to 70°. After the temperature fell, the reaction mixture was then heated on a water bath for 1 hour, and then left to stand for 48 hours at room temperature. Upon fractional distillation of the reaction mixture, there was separated 1.5 g of fraction with b.p. 145-150° (6 mm), along with a considerable quantity of lower boiling fractions:

b.p. 145-150° (6 mm); n_D^{20} 1.4910; d_4^{20} 1.0947; MR_D 68.03; calculated 68.36.

0.1445 g substance: 33.3 ml NaOH (T = 0.017841). Found %: P 11.5. $C_{12}H_{20}O_3NP$.
Calculated %: P 12.0.

SUMMARY

1. A new type of reaction – phosphonethylation – has been discovered, consisting of the addition of various nucleophilic reagents to the ethyl ester of vinylphosphinic acid.

2. By the addition of dialkylphosphorous acids, ammonia and amines to vinylphosphinic ester, there have been obtained, respectively, 1,2-di-(dialkylphosphon)-ethanes and β-diethylphosphonethylamine and its homologs.

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* See Consultants Bureau English translation, page 423.

** See Consultants Bureau English translation, page 531.

THE SYNTHESIS AND PROPERTIES OF VINYLPHOSPHINIC ESTERS

II. THE PHOSPHONETHYLATION REACTION, ADDITION OF MALONIC, CYANACETIC AND ACETOACETIC ESTERS AND THEIR HOMOLOGS TO VINYLPHOSPHINIC ESTER

A. N. Pudovik and O. N. Grishina

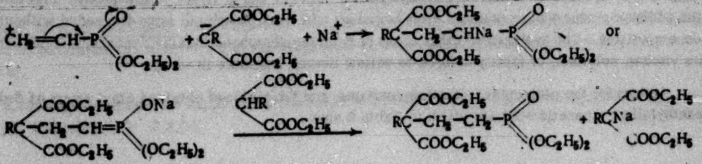
In their previous article, the authors described addition reactions of dialkylphosphorous acids, ammonia and certain secondary amines to vinylphosphinic ester. It was demonstrated that these reaction proceed very smoothly in the presence of catalysts – alcoholates of the alkali metals, and in some cases also without, by simply mixing the two substances together. As a result there were obtained a number of di-(diphosphon)-ethane esters, the ethyl ester of β-aminoethylphosphinic acid and a number of its derivatives. In view of the considerable theoretical and practical implications of the phosphonethylation reaction which has been discovered by the authors, they have proceeded to extend the investigations carried out so far, and in the present work have studied the addition reactions of malonic, cyanacetic and acetoacetic esters and their homologs, and benzyl cyanide, to vinylphosphinic ester. All of the compounds enumerated possess mobile hydrogen atoms in a methylene group, and their addition to various types of α-β-unsaturated electrophilic reagents – such as unsaturated acids and their derivatives, aldehydes, ketones, nitriles, nitrocompounds, and others – has been the object of numerous investigations for many decades. A study of the addition of malonic, cyanacetic and acetoacetic esters to unsaturated organophosphorous compounds has not been carried out up to the present time.

As in the preceding work, the authors have used the ethyl ester of vinylphosphinic acid as an unsaturated electrophilic reagent, which has been found to be the simplest and most accessible of the vinylphosphinic esters known up to the present time. All reactions have been carried out in the presence of small quantities of alkali metal alcoholates: without the use of catalysts, the reaction fails to go. It was noted that the purest products, boiling within a narrow temperature range, were obtained when sodium ethylate was used as the catalyst. When using the alcoholates of other alcohols, there is an exchange of radicals between the alcohol and the ester groups of the reactants, which ultimately leads to formation of side products and to contamination, by the same token, of the main reaction product. All of the reactions proceeded with considerable heat evolution from the reaction mixture, which, in some cases, attained 80-100°, especially upon rapid addition of the ethylate solution, and was accompanied by a violent boiling up of the reaction mixture. As preliminary experiments have demonstrated, there is no resinification of the vinylphosphinic ester; neither was there observed a decrease in the yields of addition products as compared with experiments carried out at low temperatures. Therefore, the reaction was allowed to continue further without special cooling of the reaction mixtures, but with slow gradual addition of sodium methylate. The procedural method adopted allows the reactions to be carried out easily and in a very short time.

Only one product resulted from the reaction between equimolecular quantities of malonic and of vinylphosphinic esters – the ethyl ester of β-diethylphosphonethylmalonic acid in 80% yield; under these conditions, the addition product of malonic ester to two molecules of vinylphosphinic ester was not found.

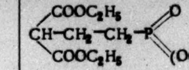
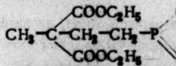
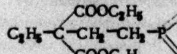
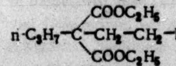
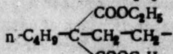
The addition of the malonic ester homologs – methyl-, ethyl-, propyl-, and n-butyl-malonic esters – to vinylphosphinic ester, in the presence of sodium ethylate, proceeds very smoothly: the corresponding ethyl esters of β-diethylphosphonethylalkylmalonic acid result in good yield. Values for the molecular refraction constants, and yields of addition products, are presented in Table 1.

The course of the addition reaction may be expressed by the following scheme:



where: R = H, CH_3, C_2H_5, n-C_3H_7, n-C_4H_9.

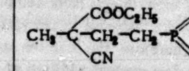
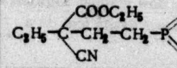
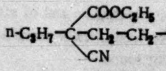
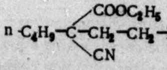
TABLE 1

No.	Formula	Boiling point	d_4^{20}	n_D^{20}	MR_D Found	MR_D Calculated	Yield (in %)
1	 $CH(COOC_2H_5)_2-CH_2-CH_2-P(=O)(OC_2H_5)_2$	158-159° (1 mm)	1.1316	1.4420	76.41	75.83	79.6
2	 $CH_3-C(COOC_2H_5)_2-CH_2-CH_2-P(=O)(OC_2H_5)_2$	175-177° (4 mm)	1.1021	1.4400	81.03	80.98	78.9
3	 $C_2H_5-C(COOC_2H_5)_2-CH_2-CH_2-P(=O)(OC_2H_5)_2$	162° (2.5 mm)	1.0925	1.4423	85.64	85.39	59.2
4	 $n\text{-}C_3H_7-C(COOC_2H_5)_2-CH_2-CH_2-P(=O)(OC_2H_5)_2$	175-176° (2 mm)	1.0782	1.4425	90.26	90.00	78.4
5	 $n\text{-}C_4H_9-C(COOC_2H_5)_2-CH_2-CH_2-P(=O)(OC_2H_5)_2$	185-186° (2.5 mm)	1.0640	1.4432	94.88	94.82	86.41

Diethylphosphonethylamalonic ester and its homologs are viscous, colorless liquids with a faint pleasant odor, insoluble in water, readily soluble in alcohol and in ether.

Two addition products — β-diethylphosphonethylcyanacetic ester, and di-(β-diethylphosphonethyl)-cyanacetic ester, resulted from reaction with cyanacetic ester upon combining equimolecular quantities of the reactants. The total yield of products was 62%. Fractional distillation of the reaction mixture was accompanied by considerable decomposition, even with the use of high vacuum, which was no doubt reflected in both the yields of products and their purity. In all of the experiments carried out, both products, and especially the di-(β-diethylphosphonethyl)-cyanacetic ester, were always yellow in color, and at times yellow-brown. Fractional distillation of the addition products of cyanacetic ester homologs with vinylphosphinic ester proceeded without visible signs of decomposition. The synthesized ethyl esters of β-diethylphosphonethylalkylcyanacetic acid were found to be quite viscous, colorless, or faintly colored to yellow liquids, insoluble in water.

TABLE 2

No.	Formula	Boiling point	d_4^{20}	n_D^{20}	MR_D Found	MR_D Calculated	Yield (in %)
1	 $CH_3-C(COOC_2H_5)(CN)-CH_2-CH_2-P(=O)(OC_2H_5)_2$	165-166° (2 mm)	1.0989	1.4430	70.28	69.96	88.9
2	 $C_2H_5-C(COOC_2H_5)(CN)-CH_2-CH_2-P(=O)(OC_2H_5)_2$	166-167° (3.5 mm)	1.0849	1.4440	74.76	74.57	66.2
3	 $n\text{-}C_3H_7-C(COOC_2H_5)(CN)-CH_2-CH_2-P(=O)(OC_2H_5)_2$	173-174° (2 mm)	1.0702	1.4443	79.28	79.19	83.7
4	 $n\text{-}C_4H_9-C(COOC_2H_5)(CN)-CH_2-CH_2-P(=O)(OC_2H_5)_2$	177-178° (3.5 mm)	1.0564	1.4460	84.16	83.81	77.7

Values for the molecular refraction constants, and the yields of obtained ethyl esters of β-diethylphosophenethylalkylcyanacetic acid are given in Table 2 above.

To prove the structure of the products obtained, one of them — the ethyl ester of β-diethylphosphonethylcyanacetic acid — was synthesized by the authors according to another method: by reacting the ethyl ester of β-bromethylphosphinic ester with the sodium derivative of ethylcyanacetic acid ester. The product obtained corresponded in its constants exactly to the ethyl ester of β-diethylphosphonethylethylcyanacetic acid as obtained by the method of the authors.

The addition of acetoacetic ester and of its homologs to vinylphosphinic ester proceeds with greater difficulty as compared with malonic and cyanacetic esters and their homologs. A considerable quantity of catalyst had to be added to the mixture, and prolonged heating applied, to promote reaction. However, even under these conditions, the yields of products remained very negligible, of the order of 15-20%; fractional distillation of the reaction mixtures was accompanied by quite considerable decomposition, with formation of considerable quantities of low-boiling products.

To conclude, the addition reaction of benzyl cyanide to vinylphosphinic ester was carried out. The reaction proceeded very vigorously, with formation chiefly of di-(β-diethylphosphonethyl)-benzyl cyanide, and only very small quantities of β-diethylphosphonethylbenzylcyanide. Total yields of both addition products consituted about 20%.

The addition of cyanacetic and acetoacetic esters, their homologs, and of benzyl cyanide to vinylphosphinic ester can be expressed by schemes similar to the one given above for the reaction with malonic ester.

EXPERIMENTAL

Addition of Malonic Ester to Vinylphosphinic Ester. A saturated solution of sodium ethylate in ethyl alcohol was added dropwise to the reaction mixture which consisted of 8.5 g of vinylphosphinic ester and 10 g of malonic ester. A strong heat evolution from the reaction mixture was observed. Following addition of the requisite quantity of ethylate necessary to complete the reaction (to the cessation of heat evolution) which proceeded for 10-15 minutes, with one hour standing at room temperature, the mixture was redistilled in vacuo. 10.5 g of the diethyl ester of β-diethylphosphonethylmalonic acid resulted (Table 1:1).

0.1564, 0.1573 g substance: 31.62, 31.82 ml NaOH (T = 0.017841). Found %: P 9.99, 9.99. $C_{13}H_{25}O_7P$. Calculated %: P 9.55.

Addition of Malonic Ester Homologs to Vinyl Phosphinic Ester. Reaction was carried out according to a procedure similar to that carried out in the preceding experiment.

Addition of Methylmalonic Ester. The reaction was carried out between 4.9 g of vinylphosphinic ester and 5.2 g of the ethyl ester of methylmalonic acid. 6 g of the diethyl ester of β-diethylphosphonethylmethylmalonic acid resulted from two fractional distillations (Table 1:2).

0.1525 g substance: 29.2 ml NaOH (T = 0.017841). Found %: P 9.46. $C_{14}H_{27}O_7P$. Calculated %: P 9.14.

Addition of Ethylmalonic Ester. 6 g of vinylphosphinic and 10 g of ethylmalonic esters were taken for reaction. 3.5 g of ethylmalonic ester was recovered during fractional distillation of the reaction mixture. There resulted 7.2 g of the ethyl ester of β-diethylphosphonethylethylmalonic acid (Table 1:3).

0.1526, 0.1528 g substance: 26.43, 26.78 ml NaOH (T = 0.017841). Found %: P 8.56, 8.66. $C_{15}H_{29}O_7P$. Calculated %: P 8.79.

Addition of Propylmalonic Ester. Reaction was carried out with 7.02 g of the ethyl ester of propylmalonic acid and 5.7 g of vinylphosphinic ester. 7.8 g of the ethyl ester of β-diethylphosphonethylpropylmalonic acid resulted (Table 1:4).

0.1508, 0.1506 g substance: 26.6, 26.5 ml NaOH (T = 0.017841). Found %: P 8.71, 8.66. $C_{16}H_{31}O_7P$. Calculated %: P 8.46.

Addition of Butylmalonic Ester. Reaction was carried out with 5.7 g of vinylphosphinic ester and 7.6 g of the ethyl ester of butylmalonic acid. 7.8 g of the ethyl ester of β-diethylphosphonethylbutylmalonic acid resulted (Table 1:5).

0.1517, 0.1524 g substance: 25.55, 25.62 ml NaOH (T = 0.017841). Found %: P 8.32, 8.30. $C_{17}H_{33}O_7P$. Calculated %: P 8.14.

Addition of Cyanacetic Ester to Vinylphosphinic Ester. 8.2 g of cyanacetic ester was added to 12 g of vinylphosphinic ester, after which a saturated solution of sodium ethylate was slowly added dropwise to the reaction mixture. Reaction proceeded very vigorously, the addition of each drop being accompanied by evolution of heat from the reaction mixture. Dropwise addition was continued for 15-20 minutes, with periodic cooling of the reaction mixture with water. Partial decomposition of the reaction mass was observed during the distillation process; condenser and receiving flasks during the distillation were filled at all times with white vapors. As the result of the first fractional distillation, three fractions were separated: 1) 65-170° (4 mm) – 2 g; 2) 170-177° (4 mm) – 4.1 g; 3) 206-255° (8 mm) – 8.8 g. As the result of repeated distillation of these three fractions, 3.1 g of the ethyl ester of β-diethylphosphonethylcyanacetic acid with b.p. 166-167° (2 mm) was obtained: n_D^{20} 1.4430; d_4^{20} 1.0740.

0.1555 g substance: 35.73 ml NaOH (T = 0.017841). Found %: P 11.35. $C_{11}H_{20}O_5NP$. Calculated %: P 11.17.

At the same time, there resulted 5.8 g of the ethyl ester of di-(β-diethylphosphonethyl)-cyanacetic acid, with b.p. 227° (2 mm): n_D^{20} 1.4540; d_4^{20} 1.3830.

0.1535, 0.1585 g substance: 45.4, 45.74 ml NaOH (T = 0.017841). Found %: P 14.61, 14.26. $C_{17}H_{33}O_8NP_2$. Calculated %: P 14.07.

Addition of Cyanacetic Ester Homologs to Vinylphosphinic Ester. Addition of Methylcyanacetic Ester. 4.8 g of the ethyl ester of methylcyanacetic acid and 6.2 g of vinylphosphinic ester were taken for reaction. Decomposition was not observed during fractional distillation of the reaction products. 5.25 g of the ethyl ester of β-diethylphosphonethylmethylcyanacetic acid resulted (Table 2:1).

0.1528, 0.1537 g substance: 31.61, 32.18 ml NaOH (T = 0.017841). Found %: P 10.22, 10.34. $C_{12}H_{22}O_5NP$. Calculated %: P 10.63.

Addition of Ethylcyanacetic Ester. Reaction was carried out with 7 g of ethylcyanacetic ester and 6 g of vinylphosphinic acid. 5.4 g of the ethyl ester of β-diethylphosphonethylethylcyanacetic acid resulted (Table 2:2).

0.1512, 0.1504 g substance: 31.36, 30.80 ml NaOH (T = 0.017841). Found %: P 10.24, 10.18. $C_{13}H_{24}O_5PN$. Calculated %: P 10.15.

Addition of Propylcyanacetic Ester. 5.6 g of propylcyanacetic ester and 5.9 g of vinylphosphinic ester were taken for reaction. As the result of repeated distillation of the reaction mixture, 4.98 g of the ethyl ester of β-diethylphosphonethylpropylcyanacetic acid was obtained (Table 2:3).

0.1521 g , 0.1490 g substance: 30.00, 29.22 ml NaOH (T = 0.017841). Found %: P 9.74, 9.69. $C_{14}H_{26}O_5PN$. Calculated %: P 9.70.

Addition of Butylcyanacetic Ester. The reaction was carried out with 6 g of vinylphosphinic ester and 5.8 g of butylcyanacetic ester. 7.95 g of the ethyl ester of β-diethylphosphonethylbutylcyanacetic acid resulted (Table 2:4).

0.1508, 0.1504 g substance: 28.54, 28.68 ml NaOH (T = 0.017841). Found%: P 9.35, 9.42. $C_{15}H_{28}O_5PN$. Calculated %: P 9.29.

Action of Sodiumethylcyanacetic Ester upon the Ethyl Ester of β-Bromethylphosphinic Acid. 5.7 g of ethylcyanacetic ester was added to an alcoholic solution of sodium ethylate prepared from 0.93 g of sodium and 14 ml of ethyl alcohol, and 10 g of the ethyl ester of β-bromethylphosphinic acid was then added dropwise. Strong heat evolution from the reaction mixture was observed. After all of the ethyl ester of β-bromethylphosphinic acid had been added, the reaction mixture was heated for 2 hours on a water bath. The precipitate of sodium bromide was filtered off, the alcohol distilled off, and the residue was redistilled in vacuo. 5.9 g of the ethyl ester of β-dieithylphosphonethylethylcyanacetic ester resulted, with b.p. 167° (4 mm): n_D^{20} 1.4440; d_4^{20} 1.0852.

Addition of Acetoacetic Ester to Vinylphosphinic Ester. A saturated solution of sodium ethylate in ethyl alcohol was added dropwise to a reaction mixture consisting of 8.9g of vinylphosphinic ester and 6.4 g of acetoacetic ester. Reaction began only after the addition of a considerable volume of alcoholic solution (1-2 ml), and there was not observed any strong evolution of heat. After 1 hour of heating on a water bath, the reaction mixture was fractionally distilled in vacuo. Fractional distillation was accompanied by considerable decomposition of the reaction mixture. After repeated fractional distillation, 2.23 g of ethyl ester of β-diethylphosphonethylacetoacetic acid with b.p. 170-172° (4 mm) resulted: n_D^{20} 1.4510.

0.1512 g substance: 30.72 ml NaOH (T = 0.017841). Found %: P 10.03. $C_{12}H_{23}O_6P$. Calculated %: P 10.53.

Addition of Propylacetoacetic Ester to Vinylphosphinic Ester. Reaction was carried out between 8.9 g of vinylphosphinic ester and 9.1g of propylacetoacetic ester. After repeated fractional distillation of the reaction mixture, 3.1 g of the ethyl ester of β-diethylphosphonethylpropylacetoacetic acid, with b.p. 138-141° (2 mm) resulted; n_D^{20} 1.4430.

0.1510, 0.1504 g substance: 30.35, 29.47 ml NaOH (T = 0.017841). Found %: P 9.93, 9.68. $C_{15}H_{29}C_6P$. Calculated %: P 9.61.

Addition of Benzyl Cyanide to Vinylphosphinic Ester. A saturated solution of sodium ethylate was added dropwise to a reaction mixture composed of 6.8 g of vinylphosphinic ester and 4.9 g of benzyl cyanide. Reaction proceeded very vigorously. The reaction mixture which was colorless at the start of the reaction became lilac in color by the end of the reaction, and also became very viscous. After a triple fractionation, accompanied by a small amount of decomposition, 1.5 g of di-(β-diethylphosphonethyl)-benzylcyanide, with b.p. 247-248° (2 mm) resulted: n_D^{20} 1.4940.

0.1510, 0.1514 g substance: 41.10, 41.24 ml NaOH (T = 0.017841). Found %: P 13.45, 13.46. $C_{20}H_{33}O_6NP_2$. Calculated %: P 13.01.

SUMMARY

It has been demonstrated that malonic, cyancetic and acetoacetic esters, and their homologs, as well as benzyl cyanide, add easily in the presence of sodium ethylate to the ethyl ester of vinylphosphinic acid, with the formation, respectively, of diethylphosphonethyl-malonic, cyanacetic and acetoacetic esters, and their homologs, and di-(β-diethylphosphonethyl)-benzylcyanide.

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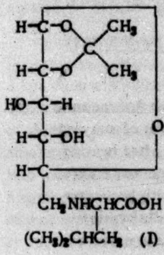
CARBOHYDRATE DERIVATIVES OF AMINO ACIDS

II. CONDENSATION OF MONOACETONEANHYDROGLUCOSE WITH LEUCINE AND GLUTAMIC ACID

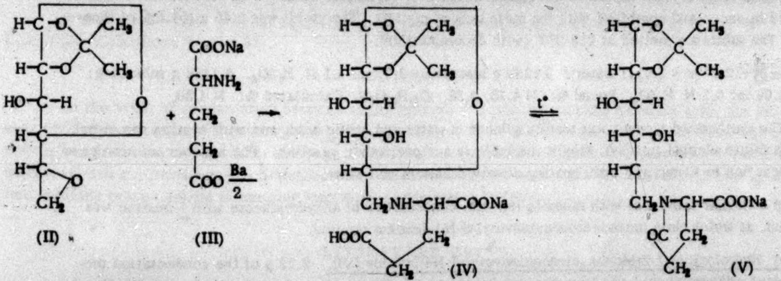
V. I. Kovalenko

As was shown in the preceding article* on the synthesis of carbohydrate-amino acid compounds, the author developed a method for condensing barium salts of amino acids with anhydroglucose. Utilizing this method, the author has condensed monoacetoneanhydroglucose with d,l-leucine, and has obtained 1,2-monoacetonequinovosyl-6-d,l-leucine (I), which precipitates in crystalline form from a hot solution after removal of the barium.



It was of interest to synthesize a carbohydrate derivative of glutamic acid which is involved in the formation of glutathione, and which plays an essential role in the construction of plant proteins. Some investigators (Abderhalden [1]) have expressed an opinion that glutamic acid bears a direct relationship to the synthesis of pyrrole compounds – both the simple [2] and the more complex [3].

By condensing anhydroglucose (II) with l-glutamic acid, taken in the form of its double sodium and barium salt (III), the author has obtained the sodium salt of 1,2-monoacetonequinovosyl-6-N-α-pyrrolidone-α′-carboxylic acid (V), instead of the sodium salt of 1,2-monoacetonequinovosyl-6-N-l-glutamic acid (IV).



This is conditioned by the fact that glutamic acid and its derivatives readily form the lactam, or an internal anhydride, frequently called α-pyrrolidone carboxylic acid [4]. V. Skola [5] established that in 2% aqueous solution, the ratio of glutamic to pyrrolidonecarboxylic acid is equal to 1:52. The high temperature and concentration of the solution displace the equilibrium to the side of the cyclic state.

Therefore, it can be considered that in the author's case, an equilibrium occurs between forms (IV) and (V), although considering the fact that isolation of substance (IV) is connected with evaporation of the solution at a temperature of 50-95°, it should be assumed that the main bulk is in the form of the sodium salt of 1,2-monoacetonequinovosyl-6-N-α-pyrrolidonecarboxylic acid.

After cleavage of the acetone radical from substances (I) and (V), quinovosyl-6-N-l-leucine (VI) and quinovosyl-6-N-α-pyrrolidone-α′-carboxylic acid (VII) resulted. (See diagram on next page).

Upon hydrolysis, compound (VII), which is affected by acetic acid, converts into (VIII), and this is related to the appearance of a mobile hydrogen atom at the nitrogen atom, with increased ability to produce colored products in acid solution when in contact with oxygen of the air. This is in conformity with the data given in the article, and also with the observation of M. Wolfrom [6]. Substances (VI) and (VII) do not mutarotate in aqueous solution.

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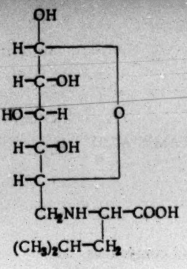
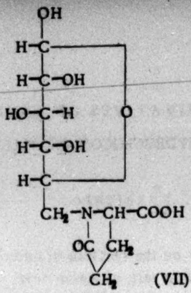
* J. Gen. Chem. 23, 86 (1953). (Consultants Bureau translation, p.83).



(VI)



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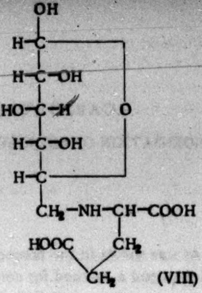

(VIII)

EXPERIMENTAL

1. Reaction of Anhydroglucose with Leucine.

a) Synthesis of 1,2-Monoacetonequinovosyl-6-N-d, l-leucine (I). 1.8 g (13.7 millimoles)of racemic leucine was dissolved by heating in 83.5 ml of 0.2 N barium hydroxide. 2.3 g (11.3 millimoles) of anhydroglucose was added. The rest of the procedure was as in the case of glycine (see Article I). After heating for 2 hours, the barium was precipitated with 35.7 ml of 0.4 N sulfuric acid and the hot solution was filtered through a funnel constructed for hot filtering. The sediment on the filter was washed twice with hot water (using 20-25 ml portions) and the wash waters collected separately. After cooling, white, needle crystals separated; filtered, washed with absolute alcohol and ether, and the filtrate tested for complete barium precipitation, and if absent, vaporized in vacuo together with the wash waters, to a volume of 20-25 ml. After cooling, large crystals separated out again, which were separated, washed with alcohol and ether, and then dried in vacuo and combined with the main bulk of crystals. The yield was 2.45 g (51.8% of theoretical). The substance melted at 218-220° (with decomposition).

$[\alpha]_D^{24}$ −12.6° (c = 1.011; water). 0.1230 g substance: 3.67 ml 0.1 N H_2SO_4. 0.1438 g substance: 4.09 ml 0.1 N H_2SO_4. Found %: N 4.18, 3.98. $C_{15}H_{27}O_7N$. Calculated %: N 4.20.

The synthesized product was readily soluble in water and acetic acid, and with heating somewhat soluble in dilute alcohol (methyl, ethyl), insoluble in acetone, ether, gasoline. The aqueous solution gave an acid reaction to litmus and upon heating dissolved barium carbonate.

In a similar fashion,as with racemic leucine, condensation of anhydroglucose with l-leucine was carried out, at which time monoacetonequinovosyl-6-N-l-leucine resulted.

b) Hydrolysis of 1,2-Monoacetonequinovosyl-6-N-l-leucine (VI). 2.12 g of the condensation product between anhydroglucose and l-leucine was heated in a hydrogen atmosphere for 3.5 hours with 53 ml of 50% acetic acid, proceeding then as in the case of glycine. The residue in the flask was dissolved by heating in 50 ml of absolute ethanol, from which light-brown crystals precipitated out upon cooling. Filtered and washed with absolute isopropyl alcohol. Yield was 0.28 g (15.6% of theoretical). The substance melted at 208-210° (with decomposition). After decolorization of the filtrate with carbon, followed by evaporation at room temperature in an open beaker to a volume of 5-8 ml, there resulted another 0.5 g of the product. Quinovosyl-6-N-l-leucine is soluble in water, dilute methyl and ethyl alcohols, insoluble in absolute isopropyl alcohol, acetone, chloroform and pyridine.

$[\alpha]_D^{22}$ + 33.7° (c = 0.861; water).

0.1322 g substance: 4.36 ml 0.1 N H_2SO_4. 0.0966 g substance: 3.14 ml 0.1 N H_2SO_4. Found %: N 4.62, 4.59. $C_{12}H_{23}O_7N$. Calculated %: N 4.77%.

2. Reaction between Anhydroglucose and Glutamic Acid.

a) Synthesis of the Sodium Salt of 1,2-Monoacetonequinovosyl-6-N-α-pyrrolidone-α"-carboxylic acid (V). The double barium and sodium salt of glutamic acid was prepared by dissolving 1.1 g (6.5 millimoles)of sodium glutamate in 30 ml of 0.2 N-barium hydroxide. 1.2 g (6 millimoles) of anhydroglucose was added to the resulting solution. The solution was heated under reflux for one hour, an equivalent quantity of sulfuric acid (16.3 ml of 0.4 N) was added to the hot solution, filtered, and tested for complete precipitation of barium. The filtrate was evaporated in vacuo at a bath temperature of 50-60°, and the residue in the flask then dried for several minutes at 95-100°. The contents of the flask were then dissolved in 12 ml of methanol with heat, and the reaction product precipitated with 6 ml of dry acetone. The precipitate was filtered rapidly and washed with dry acetone. It was obtained in the form of a white, very hygroscopic powder, readily soluble in water, aqueous alcohol, insoluble in acetone, ether, benzene, chloroform. Yield 1.14 g, or 45.8% of theoretical.

$[\alpha]_D^{24} -6.5°$ (c = 3.43; water).

After prlonged drying in a desiccator, the substance melted at 160-163°.

0.1696 g substance: 4.88 ml 0.1 N H_2SO_4. 0.1594 g substance: 4.60 ml 0.1 N H_2SO_4. 0.1210 g substance: 0.239 g Na_2SO_4. 0.1346 g substance: 0.268 g Na_2SO_4. Found %: N 4.02, 4.04. Na 6.40, 6.43. $C_{14}H_{20}O_8NNa$. Calculated %: N 3.96; Na 6.51.

b) Hydrolysis of Sodium 1,2-Monoacetonequinovosyl-6-N-α-pyrrolidone-α'-carboxylate. 1.46 g of sodium 1,2-monoacetonequinovosyl-6-N-α-pyrrolidone-α'-carboxylate dissolved in 25 ml of 50% acetic acid was heated 3.5 hrs. in a hydrogen atmosphere. The procedure was further carried out as described in article I. The residue in the flask, which consisted of the amorphous substance and sodium acetate, was ground well with 5 ml of dry acetone and 5 ml of absolute methanol, filtered, the filtrate evaporated in vacuo, and then dissolved with gentle heating in 4 ml of absolute methanol, and filtered again if necessary, and the solution mixed with 10 ml of absolute ether. The solution was poured off from the resulting viscous oil and the oil dried over sulfuric acid in a vacuumdessicator. A very hygroscopic powder results, readily soluble in water and alcohols and insoluble in other solvents. The aqueous solution of quinovosyl-6-N-α-pyrrolidonecarboxylic acid possessed an acid reaction toward litmus. The product melted at 120-130° and did not give a color with aqueous ninhydrin solution. Yield was 0.8 g (66% of theoretical).

$[\alpha]_D^{26}$ + 26.5° (c = 1,284; water).

0.1368 g substance: 4.58 ml 0.1 N H_2SO_4. 0.1242 g substance: 4.10 ml 0.1 N H_2SO_4. Found %: N 4.68, 4.62. $C_{11}H_{17}O_8N$. Calculated %: N 4.82.

SUMMARY

As the result of condensation between anhydroglucose and leucine and with glutamic acid, the following have been obtained: monoacetonequinovosyl-6-l-leucine and the sodium salt of monoacetonequinovosyl-6-N-α-pyrrolidone-α''-carboxylic acid, and after cleavage of acetone there has been separated: quinovosyl-6-N-l-leucine and quinovosyl-6-N-α-pyrrolidone-α'-carboxylic acid, which represents carbohydrate derivatives of amino acids with a free reducing group capable of entering into various chemical reactions.

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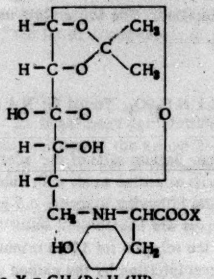
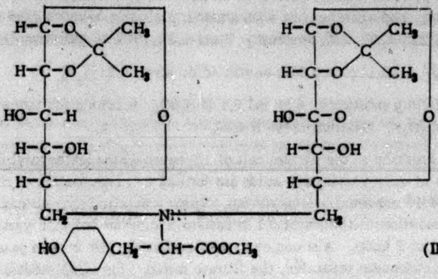
CARBOHYDRATE DERIVATIVES OF AMINO ACIDS

III. CONDENSATION OF ANHYDROGLUCOSE WITH TYROSINE

M. Kh. Gluzman and V. A. Kovalenko

In the preceding articles the authors have described a synthesis for aliphatic quinovosylamino acids, derived from glycine, leucine and glutamic acid. It will be shown in the present work that when anhydroglucose is condensed with the methyl ester of tyrosine, there result the methyl esters of monoacetonequinovosyl-6-N-1-tyrosine (I) and bis-(monoacetonequinovosyl-6-6')-N-1-tyrosine (II). Condensation with the barium salt of tyrosine also proceeds readily: from the barium salt of monoacetonequinovosyl-6-N-1-tyrosine a free acid (III) was separated:





(II)

where X = CH_3(I); H (III).

Three functional groups are contained in the tyrosine molecule (COOH, OH, NH_2), which are able to add to the ethylene oxide ring of anhydroglucose. The separation of the barium salt of monoacetonequinovosyl-6-N-tyrosine as the principal reaction product indicated that the carboxyl group does not participate in this reaction.

In the case of phenolic hydroxyl addition to the ethylene oxide ring of anhydroglucose, a phenol ester should have resulted. However, compounds (I), (II) and (III) gave the Millon reaction, indicating the presence of free phenolic hydroxyl in tyrosine [1].

Theratio of quinovosyl derivatives of tyrosine and its methyl ester to diazobenzenesulfoacid may serve as indirect confirmation of the fact that compounds (I), (II) and (III), as obtained by the authors, possess the structures which have been ascribed to them. It is known that tyrosine and its esters will couple with diazobenzenesulfoacid [2] to form a red dye. If, however, tyrosine is benzoylated, then its ability to couple disappears [3]. The authors have observed a red coloration upon combining diazobenzenesulfoacid in soda solution with the quinovosyl derivative of tyrosine and its methyl ester, but after treating substances (I), (II) and (III) with benzoyl chloride, they no longer enter into azo linkage reaction. It is obvious that if condensation between anhydroglucose and tyrosine (and its ester) were to be accomplished at the expense of the phenolic hydroxyl, then conjugation with diazobenzenesulfoacid should have occurred after benzoylation also, since alkylated phenols enter into azo conjugation on reactions.

As the result of cleavage of the acetone group from compound (III), quinovosyl-6-N-1-tyrosine resulted, readily soluble in water, differing from the initial tyrosine wich is difficultly-soluble in water.

EXPERIMENTAL

a) Synthesis of 1,2-monoacetonequinovosyl-6-N-1-tyrosine(III); 56 ml of 0.2 N barium hydroxide was added to a suspension of 2.18 g (12 millimoles) of tyrosine in 300 ml of water and heated to complete solution of tyrosine. 2.24 g (11 millimoles) of anhydroglucose was added to the resulting solution and heated on a boiling water bath with reflux for 2 hours. The remainder of the procedure was as described in the general methods [4]. After evaporating the filtrate, the residue was boiled with 10 ml of water, filtered, washed with cold water, methyl and ethyl alcohols.

After drying 3 hours at 50-60°, the substance melted at 233-234° (with decomp.) The yield was 3 g (70.7% of theoretical). The reaction product – 1,2-momoacetonequinovosyl-6-N-l-tyrosine, was poorly soluble in water (1 part in 400 parts of water), ethyl, methyl alcohols and other organic solvents, more readily soluble in formic and acetic acids, and readily soluble in alkali and in mineral acids.

$[\alpha]_D^{22}$ – 27.7° (c = 0.267; water).

0.1418 g substance: 3.54 ml 0.1 N H_2SO_4. 0.1029 g substance: 2.61 ml 0.1 N H_2SO_4. Found %: N 3.50, 3.55. $C_{18}H_{25}O_8N$. Calculated %: N 3.65

The substance gave positive diazo reaction and also Millon reaction, and reduced Fehling's solution only after acid hydrolysis. The aqueous solution gave an acid reaction with litmus.

b) Hydrolysis of 1,2-monoacetonequinovosyl-6-N-l-tyrosine (III). 2 g of product (III) was dissolved, with heating, in 120 ml of 50% acetic acid and the hydrolysis was carried out for 3 hours according to the general procedure. After evaporation of the solvent and removal of the acetic acid, the residue in the flask was then boiled with 15 ml of acetone, ethyl acetate, 10 ml of 96% alcohol, and then with 10 ml of methyl alcohol. Filtered, washed with alcohol, ether and dried in a vacuum-desiccator. The resulting quinovosyl-6-N-l-tyrosine was a fine crystalline powder, slightly yellow in color, soluble in water, acetic acid, pyridine. Easily reduced Fehling solution upon heating, and upon heating with aqueous ninhydrin solution gave a violet coloration. The Millon test was positive. M.p. 215-220° (with decomp.) Yield 1.2 g (67% of theoretical).

$[\alpha]_D^{21}$ + 40.1° (c = 0.366; acetic acid: water = 2:1).

0.1476 g substance: 4.23 ml 0.1 N H_2SO_4. 0.1089 g substance: 3.10 ml 0.1 N H_2SO_4. Found %: N 4.01: 3.98. $C_{15}H_{21}O_8N$. Calculated %: N 4.07.

c) Isolation of the barium salt of 1,2-monoacetonequinovosyl-6-N-l-tyrosine. Barium salts of the acetone derivatives of quinovosylamino acids are formed by condensation of the barium salts of amino acids with anhydroglucose and do not usually separate out. Their separation may be carried out in the following manner: 0.7 g of l-tyrosine solution in 100 ml of 0.1 N barium hydroxide and 0.75 g of anhydroglucose are heated on a water bath with reflux for 2 hours. A strong current of carbon dioxide is then passed through the solution for 10-15 minutes, the barium carbonate separated, the filtrate tested for completeness of barium precipitation by the carbon dioxide, then evaporated to dryness at 60-70° in vacuo. The barium salt remaining in the flask was boiled with 15 ml of water. Filtered and dried. Yield 1.09 g (62% of theoretical). The barium salt decomposes at 215-220° and gives a positive diazo reaction.

$[\alpha]_D^{22}$ + 39.7° (c = 0.159; water).

0.1323 g substance: 0.0343 g $BaSO_4$. 0.1556 g substance: 0.0403 g $BaSO_4$. Found %: Ba 15.25, 15.24. $C_{36}H_{48}O_{16}N_2Ba$. Calculated %: Ba 15.22.

d) Synthesis of the methyl ester of 1,2-monoacetonequinovosyl-6-N-l-tyrosine (I). A well-ground mixture of equimolecular quantities of anhydroglucose (2 g) and the methyl ester of tyrosine (1.95 g), obtained by the method of E. Fischer [5], was heated in a hard glass test tube on a glycerol bath at 110-115° for 10 minutes. 30 ml of water was gradually added to the melt, cooled to 90°, and well stirred with a rod. The homogeneous solution was left 24 hours at room temperature, and the solvent was evaporated on a water bath to a residual volume of 8-10 ml. After cooling, crystals separated, were filtered off, washed with cold water, alcohol, acetone, and dried in a desiccator. Yield 2.4 g (61% of theoretical). The melting point of the methyl ester of monoacetonequinovosyl-6-N-l-tyrosine was 232-234°. It was insoluble in actone, benzene, ether, dichlorethane, nitrobenzene, pyridine, acetic acid and pyridine-water mixture; partially soluble in hot water, soluble in formic acid. Gave a positive Millon reaction.

$[\alpha]_D^{26}$ + 14.8° (c = 1.217; absolute formic acid).

0.1217 g substance: 3.03 ml 0.1 N H_2SO_4. 0.1400 g substance: 3.46 ml 0.1 N H_2SO_4. Found %: N 3.49,3.46. $C_{19}H_{27}O_8N$. Calculated %: N 3.52.

Upon fusing the methyl ester of tyrosine with anhydroglucose in the presence of pyridine, the reaction became accelerated so much that the resulting methyl ester of 1,2-monoacetonequinovosyl-6-N-l-tyrosine was markedly contaminated by resinification products of anhydroglucose, resulting from the sharp temperature rise of the melt because of the reaction heat evolved.

e) Synthesis of the methyl ester of bis-(monoacetonequinovosyl-6,6'-)-N-l-tyrosine (II). A well-ground mixture of 0.8 g of monoacetoneanhydroglucose and 0.39 g of the methyl ester of tyrosine was heated for 1-1.5

minutes at 100°. The mixture formed rapidly a yellow melt, which was dissolved in 15 ml of water and decolorized with carbon. The water was evaporated in vacuo at 50-60°, the residue boiled with 10 ml of dry benzene, and then with 15 ml of dichlorethane. After filtration, the product was dissolved in 8 ml of absolute ethanol and precipitated with 15 ml of dry ether. It was filtered, washed with ether, and dried in a vacuum-desiccator. The light yellow, very hygroscopic substance was soluble in water and especially in aqueous alcohols; insoluble in the usual dry organic solvents. It decomposed at 100-110°. Yield was 1 g (83% of theoretical).

$[\alpha]_D^{20}$ −5.2° (c = 1.922; water).

0.1856 g substance: 2.90 ml 0.1 N H_2SO_4. 0.2863 g substance: 4.35 ml 0.1 N H_2SO_4. Found %: N 2.19, 2.13. $C_{28}H_{43}O_{13}N$. Calculated %: N 2.33

The aqueous solution of synthesized methyl ester of bis-(monoacetonequinovosyl-6,6')-N-l-tyrosine acquired a red-brown coloration upon heating with a 1% aqueous solution of ninhydrin. The Millon and diazo reactions were positive.

All synthesized tyrosine derivatives in soda solution gave positive diazo reactions, which consisted in the appearance of a red color upon combining a soda solution of the tyrosine derivative with diazobenzenesulfoacid solution. However, if 0.01-0.02 g of any of the tyrosine derivatives obtained by the authors were mixed with 4-5 ml of saturated soda solution, 3-4 drops of benzoyl chloride added and allowed to stand for several hours until the odor of the latter disappeared, then such benzoylated products no longer gave reaction with diazobenzenesulfoacid.

SUMMARY

1. It has been demonstrated that when monoacetoneanydroglucose is condensed with the barium salt of tyrosine, addition of the amino acid to the ethylene oxide ring of anhydroglucose proceeds at the expense of the amino groups, and not at the expense of the carboxyl and hydroxy groups.

2. The ethyl ester of bis-(monoacetonequinovosyl-6,6')-N-l-tyrosine, monoacetone-l-quinovosyl-6-N-l-tyrosine, and also quinovosyl-6-N-l-tyrosine and its barium and acetone derivatives have been synthesized.

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* See Consultants Bureau English translation, page 83.

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SUMMARY

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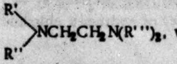
THIAZOLYL DERIVATIVES OF ETHYLENE- AND TRIMETHYLENE-DIAMINE. I.

S. G. Fridman

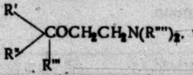
At the present time the cause of a variety of allergic ailments is generally accepted as being due to histamine. Elucidation of the role of histamine has served to stimulate development of intensive research work in the field of synthesis of compounds possessing antihistaminic properties. Within the past few years a large number of such compounds have been synthesized. Fundamentally, these compounds may be divided into two groups, namely:

1) Ethylenediamine derivatives of the type:



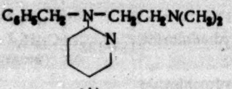
$\begin{matrix} R' \\ R'' \end{matrix}\!\!>NCH_2CH_2N(R''')_2$, where $R'=C_6H_5$, $C_6H_5CH_2$; $R''=C_6H_5$ or the hetero-cyclic radical (pyridyl, pyramidyl, furfuryl, imidazolyl and others); $R'''=CH_3$ or $N(R''')_2$ = the pyridine radical, pyrimidine, and so forth.

2)Ethanolamine derivatives of the type:

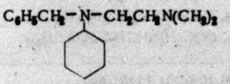


$\begin{matrix} R' \\ R'' \end{matrix}\!\!>\underset{R'''}{C}OCH_2CH_2N(R'''')_2$, where $R'=C_6H_5$; $R''=C_6H_5CH_2$, p-$CH_3OC_6H_4CH_2$, cyclohexyl; $R'''=$ H, CH_3; $R''''=CH_3$ or $N(R'''')_2$ = a pyridine group, morpholine, and so forth.

Derivatives of asymmetrically-substituted ethylenediamine with the pyridine ring as substituent R'' are considerably more active than compounds with the phenyl radical as R''; Thus, for example, pyribenzamine (A) is many times more active than anthergane (B):

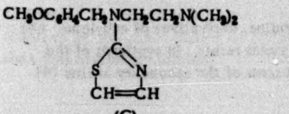


(A)



(B)

In some medicinal preparations, for example, in sulfidine, the pyridine radical can be successfully replaced by the thiazole radical, while at the same time less toxic compounds result. It was therefore of interest to the authors to synthesize a number of new substances analogous to those of known antihistaminics of the ethylenediamine series, in which the pyridine radical would be replaced by the thiazole radical.



(C)

When the authors started their work, there were no compounds described in the literature that contained the thiazole ring in the molecule of an asymmetrically-substituted ethylenediamine. Such ethylenediamine derivatives are now known [1,2].

There exists indication that N,N-dimethyl-N'-(p-methoxybenzyl)-N'-(2-thiazolyl)-ethylenediamine (C) possesses powerful antihistaminic action.

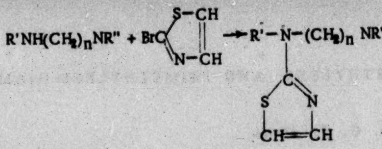
The following procedure was set up for the synthesis of thiazolyl derivatives of ethylene- and trimethylethylene-diamine derivatives.

1. To condense the primary aryl or aralkylamines with dialkylaminoalkylbromides to obtain secondary dialkylaminoalkylaryl (or aralkyl) amines according to the scheme:

$$R'NH_2 + Br(CH_2)_nNR'' \rightarrow R'NH(CH_2)_n\ NR'',$$

where $R' = C_6H_5$, $C_6H_5CH_2$; $R''=CH_3$ or $N(R'')_2$ = piperidyl;. n = 2 or 3.

2. To condense with 2-bromthiazole in pyridine according to the scheme:



The author has obtained a series of secondary dialkylaminoalkyl- or aralkylamines, as given in the table. (I) was obtained according to the method given for it in the literature [4]. Preparation (V) has been synthesized for the first time from N-benzyl-benzamide [5]; the author obtained it, in a manner similar to preceding preparation (I), from benzylamine and the hydrobromide of dimethylaminoethylbromide in the presence of potash, in 30% yield of theoretical. Preparation (VI) was obtained by condensing γ-dimethylaminopropylamine with p-methoxybenzylchloride in pyridine.

The secondary amides were colorless liquids, with the exception of preparation (IV), melting at 44°. They formed nicely-crystallizing dihydrochlorides on treatment with the calculated quantity of hydrogen chloride in ether solution.

Preparations (III) and (IV), having electronegative substituents in the para-position of the benzene ring, form only the monohydrochlorides and monopicrates. This is apparently explained by the fact that electronegative substituents in the para-position weaken the basicity of the nitrogen atom bound to the benzene ring, with resulting loss in ability to add a proton: the salt is therefore only formed by the dimethylamino group.

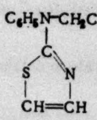
TABLE

preparation no.	structure	boiling point	yield (%)	melting point		empirical formula
				dihycrochloride	picrate	
(I)	$C_6H_5NHCH_2CH_2N\ CH_3)_2$	100-105°(6 mm)	70	176-177°	–	–
(II)	p-$C_2H_5OC_6H_4NHCH_2CH_2NC_5H_{10}$	173-175°(3 mm)	60	174	–	$C_{15}H_{24}ON_2 \cdot 2HCl$
(III)	p-$C_2H_5COOC_6H_4NHCH_2CH_2N(CH_3)_2$	181-185° (4 mm	32	Monohydrochloride 159-161	137-138°	$C_{19}H_{23}O_9N_5$ (picrate)
(IV)	p-$BrC_6H_4NHCH_2CH_2NC_5H_{10}$	180-181°(4 mm) m.p. 44°	32	Monohydrochloride 208	–	$C_{13}H_{19}N_2Br \cdot HCl$
(V)	$C_6H_5CH_2NHCH_2CH_2N(CH_3)_2$	115-117°(4 mm)	30	205-207	–	–
(VI)	p-$CH_3OC_6H_4CH_2NHCH_2CH_2CH_2N(CH_3)_2$	155-160°(4 mm)	43	188-189	–	$C_{13}H_{22}ON_2 \cdot 2HCl$

Upon boiling dialkylaminoalkylarylamines with 2-bromothiazole in pyridine, derivatives of ethylene- and trimethylenediamine are formed with thiazole radicals as substituents. Small yields result. In synthesis of the analogous pyridine derivatives, it is possible to increase the yield by using an excess of the secondary amine [6]. In the case of the thiazole derivatives this is ineffective.

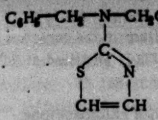
Upon fractionally distilling the reaction mixture in vacuo, the condensation product did not result in pure form; the author therefore purified the bases by means of the perchlorates. Thus, the following preparations resulted:

1. N,N-Dimethyl-N'-phenyl-N'-(2-thiazolyl)ethyenediamine (VII);

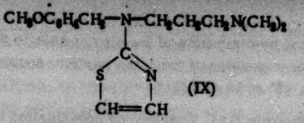


(VII)

2. N,N-Dimethyl-N'-benzyl-N'-(2-thiazolyl)-ethylenediamine (VIII); 3. N,N-Dimethyl-N'-(p-methoxybenzyl)-N'-(2-thiazolyl)-trimethylenediamine (IX): (see top of next page)



(VIII)

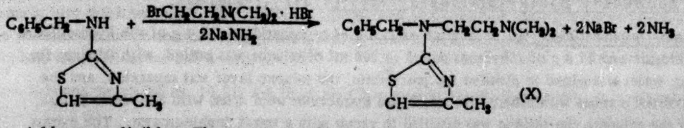


(IX)

Under the conditions indicated (boiling in pyridine), N,N-dimethyl-N'-(carbethoxyphenyl)-ethylenediamine (III) and N-(β-piperidinoethyl)-p-bromoaniline (IV) do not condense with 2-bromothiazole.

The conclusion might be drawn therefore that the mobility of the hydrogen atom of the secondary amino group bound to the benzene ring, in the para position of which is present a negative substituent, decreases sharply.

Upon interacting the hydrobromide of dimethylaminoethylbromide with 2-benzylamino-4-methylthiazole, there resulted accordingly, N,N-dimethyl-N'-benzyl-2-(4-methylthiazolyl)-ethylenediamine (X), in conformity with the equation:



$$C_6H_5CH_2{-}NH + \xrightarrow[2NaNH_2]{BrCH_2CH_2N(CH_3)_2 \cdot HBr} C_6H_5CH_2{-}N{-}CH_2CH_2N(CH_3)_2 + 2NaBr + 2NH_3$$

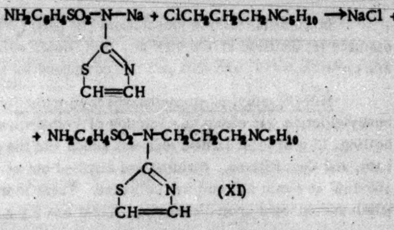
(X)

The yield was negligible. The reaction product was identified in the form of the perchlorate with m.p. 144°.

TABLE

Nitrogen (in %)		Chlorine (in %)	
Found	Calculated	Found	Calculated
–	–	–	–
8.95, 8.96	8.72	–	–
14.82, 14.97	15.05	Monohydrochloride 12.97,12.95	13.12
9.00, 9.13	8.80	11.10, 11.31	11.11
–	–	–	–
9.56,9.62	9.49	23.91,23.92	24.06

Upon boiling the sodium salt of 2-p-aminobenzenesulfamidothiazole with γ-piperidinopropylchloride, preparation (XI) resulted in almost quantitative yield, according to the equation:



$$NH_2C_6H_4SO_2{-}N{-}Na + ClCH_2CH_2CH_2NC_5H_{10} \rightarrow NaCl + NH_2C_6H_4SO_2{-}N{-}CH_2CH_2CH_2NC_5H_{10}$$

(XI)

Preparations (VII), (X), and (XI) were tested pharmacologically. It was found that they all possessed antihistaminic action to a greater orlesser degree. The most active was found to be preparation (X), which seems to be the exact analog of pyribenzamine (A). However, the activity of (X) is considerably weaker than that of pyribenzamine.

EXPERIMENTAL

I. Synthesis of the Original Substances.

Hydrobromide of dimethylaminoethylbromide. This was obtained by the method proposed for the hydrobromide of β-bromoethylamine [7]. The crude product was obtained from 142.4 g of dimethylaminoethanol and 700 ml of hydrobromic acid of specific gravity 1.42. The solid residue remaining in the flask after distilling off the hydrobromic acid was thoroughly ground with 350 ml of acetone, filtered off, washed with a small quantity of cooled acetone and dried with ether. The yield was 297 g, 80% of theoretical; m.p. 289°.

Hydrochloride of β-piperidinoethylchloride. This was obtained from piperidinoethanol and thionyl chloride in chloroform solution [8]; m.p. 229-231°.

γ-Piperidinopropylchloride. Obtained from trimethylenechlorobromide and piperidine in ether solution [9]. Distilled at 68-70° and 4 mm.

p-Methoxybenzylchloride. Obtained from anisole, formalin and gaseous hydrogen chloride in the presence of zinc chloride [10]; b.p. 105-110° at 8 mm (literature data 115-120° at 16 mm).

2-Bromothiazole. Obtained by dinitration of 2-aminothiazole in phosphoric acid medium in the presence of nitric acid, with subsequent decomposition of the diazo solution, according to Sandmeyer [11]. Distilled at 74° and 22 mm (literature data, b.p. 69° at 16 mm [11]).

2-Benzylamino-4-methylthiazole [12]. Obtained by condensation of benzylthiourea with chloroacetone. A mixture of 5 g of benzylthiourea and 2.5 ml of chloroacetone (excess) was heated on a water bath for 1 hour. The reaction product was then dissolved in water, and excess chloroacetone extracted with ether. The aqueous solution was alkalized with 10% caustic soda solution, and the precipitated 2-benzylamino-4-methylthiazole was filtered off, washed with water and recrystallized from aqueous methyl alcohol. M.p. 98°; picrate m.p. 192-194°; which corresponded to the literature data. Yield 5.5 g; 90% of theoretical.

The same product was obtained by condensation of 2-amino-4-methylthiazole with benzyl chloride. The yield amounted to 15% of the theoretical.

II. Synthesis of Secondary Dialkylaminoalkylaryl-(aralkyl)-amines.

N-β-Piperidinethyl-p-phenetidine (II). A mixture of 27.4 g of p-phenetidine, 18.4 g of the hydrochloride of β-piperidinoethylchloride and 27.6 g of anhydrous potash in 100 ml of toluene was boiled, with stirring, for 8 hours. After cooling, water was added to dissolve the precipitate, the toluene layer was separated, and the aqueous layer was extracted 3 times with ether. The combined extractions were dried with anhydrous potash, and after distilling off the solvents, the residue was distilled in vacuo with a spiral dephlegmator. The excess p-phenetidine distilled off first, and then the secondary amine was collected at 173-175° and 3 mm. The yield was 14.8 g, 60% of theoretical.

The dihydrochloride resulted on dissolving the amine in absolute ether and adding to the solution the calculated quantity of hydrogen chloride in ether solution. The white precipitate which formed was recrystallized from absolute alcohol; m.p. 174°.

In a similar fashion preparations (I), (III), (IV) and (V) were obtained. N,N-Dimethyl-N'-phenylethylenediamine (I) distilled at 100-105° at 6 mm, which coincides with the data of Leonard and Solmssen [4]. Huttrer and co-workers [13] who obtained this compound for the first time indicated a b.p. of 103-107° at 0.2 mm.

N-N-Dimethyl-N'-(p-methoxybenzyl)-trimethylenediamine (VI). 12.6 g of freshly-distilled p-methoxybenzylchloride was added to a solution of γ-dimethylaminopropylamine in 20 ml of pyridine. After 15 hours boiling, 15 g of solid caustic soda was added and the mixture was heated for another 30 minutes on a water bath, and then filtered. Pyridine was distilled out of the filtrate, and the residue was redistilled in vacuo. The 155-160° at 4 mm fraction was collected. There remained in the distilling flask some higher-boiling liquid, which decomposed upon distillation. Yield was 9.5 g, 45% of theoretical.

The dihydrochloride was obtained as with the preceding; m.p. 188-189°.

III. Synthesis of 2-Thiazolyl Derivatives of Ethylene- and Trimethylenediamine.

N,N-Dimethyl-N'-phenyl-N-(2-thiazolyl)-ethylenediamine (VII). 5.5 g of 2-bromothiazole was added to a solution of 5.5 g of N,N-dimethyl-N'-phenylethylenediamine (I) in 10 ml of pyridine, and the mixture was boiled on reflux for 12 hours. 10 g of solid caustic soda was then added and the mixture boiled on a water bath for 20 minutes. The solution was filtered off from the solid residue, and after distilling off the pyridine, the residue was redistilled in vacuo. The fraction boiling at 145-150° at 5 mm was collected. Yield was 1.45 g. An almost colorless liquid. Gave a perchlorate which was recrystallized from alcohol, m.p. 199°.

Found %: N 8.89, 8.95. $C_{13}H_{17}N_3S \cdot HClO_4$. Calculated %: N 9.20.

N,N-Dimethyl-N'-benzyl-N'-(2-thiazolyl)-ethylenediamine (VIII). Obtained from 6.5 g of N,N-dimethyl-N'-benzylethylenediamine (V) and 3.3 g of 2-bromothiazole in a manner similar to the preceding. The fraction boiling at 183-185° at 5 mm was collected. The yield was 2.1 g, 40% of theoretical, calculating on the basis of 2-bromothiazole.

As has already been mentioned, this compound is described in patent [2], where the melting point of the picrate is given. Since the authors could not obtain the picrate in crystalline form, the base was therefore identified in the form of the perchlorate, which, after recrystallization from alcohol, represented colorless needles with m.p. 139°.

Found %: N 11.50, 11.42. $C_{14}H_{19}N_3S \cdot HClO_4$. Calculated %: N 11.61.

N,N-Dimethyl-N'-(p-methoxybenzyl)-(2-thiazolyl)-trimethylenediamine (IX). Obtained from 8.9 g of N,N-dimethyl-N'-(p-methoxybenzyl)-trimethylenediamine (VI) and 3.2 g of 2-bromothiazole in pyridine, similarly to the preceding. After distilling off the solvent, the residue was redistilled in vacuo at 3 mm. The resulting fractions: I) 155-160° – 5.1 g (initial analysis); II) 160-170° – 0.5 g; III) 170-195° – 2.2 g. The third fraction was redistilled in vacuo once more, and the portion boiling at 185°-190° at 3 mm was collected.

Unfortunately, the author failed to obtain the crystalline hydrochloride; picrate or perchlorate. Analysis of the distillation product gave low nitrogen and sulfur content. Likewise, the condensation product from N-(β-piperidinoethyl)-p-phenetidine and 2-bromothiazole failed to separate in the pure form.

N,N-Dimethyl-N'-benzyl-N'-2-(4-methylthiazolyl)-ethylenediamine, (X). A mixture of 9.6 g of 2-benzylamino-4-methylthiazole and 4.6 g of sodamide in 75 ml of toluene was boiled for 2 hours. 14 g of the hydrobromide of dimethylaminoethylbromide was added to the cooled solution, and the mixture was boiled for another 12 hours. After cooling, the precipitate was filtered off, the toluene distilled off, and the residue distilled in vacuo at 10 mm. Everything distilled in the range 173-195°. It failed to separate into fractions, the distillate being a very thick viscous mass. Upon treating the distillate with 30% chloric acid, it was possible to separate the perchlorate in the form of large prisms, readily soluble in hot alcohol and water. After recrystallization from alcohol, the perchlorate had a m.p. of 144°.

Found %: N 10.98, 10.91; S 8.75, 8.91; Cl 9.29, 9.36. $C_{15}H_{21}N_3S \cdot HClO_4$. Calculated %: N 11.18; S 8.52; Cl 9.45.

Upon action of aqueous sodium carbonate solution on the perchlorate, the base separated out in the form of a colorless oily liquid. It was extracted with ether, the ether extract dried with sodium sulfate, and after distilling off the ether, the oil did not crystallize. The oil dissolved in absolute ether, and to the solution was added the calculated quantity of hydrogen chloride in ether. The resulting precipitate was filtered off rapidly, washed with ether and dried in a vacuum desiccator. The resulting dihydrochloride was very hygroscopic.

N-(2-Thiazolyl)-N-(γ-piperidinopropyl)-p-aminobenzenesulfamide (XI). 3.2 g of γ-piperidinopropylchloride was added to an alcoholic solution of 5.55 g of the sodium salt of 2-(p-aminobenzenesulfamide)-thiazole and the mixture heated for 3 hours. The resulting sodium chloride precipitate was filtered off, and the alcohol was distilled off from the filtrate. The residue was recrystallized from alcohol: m.p. 180°. Yield almost quantitative.

Found %: N 14.86, 15.01; S 16.86, 17.07. $C_{17}H_{24}O_2N_4S_2$. Calculated %: N 14.73; S 16.84.

The base gave only a monohydrochloride: m.p. 203-205°.

Found %: Chlorine ion 8.61, 8.82. $C_{17}H_{24}O_2N_4S_2 \cdot HCl$. Calculated %: Chloride ion 8.52.

The author expresses his appreciation to Active Member of the Academy of Science of the Ukrainian SSR, Professor A. I. Kiprianov, for his valuable advice in the work.

SUMMARY

1. Four new secondary dialkylaminoalkylarylamines have been synthesized.

2. A symmetrically-substituted ethylene- and trimethylene-diamines, containing the thiazole radical as substituent, have been described.

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THIAZOLYL DERIVATIVES OF ETHYLENE- AND TRIMETHYLENE-DIAMINE. II.

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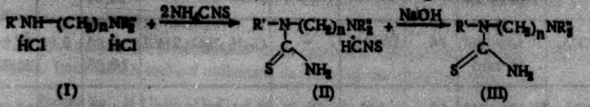
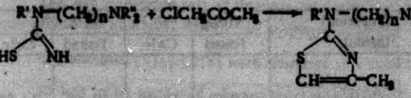
In the preceding work [1] 2-thiazolylsubstituted ethylene- and trimethylene-diamine were described, obtained either by introduction of the thiazole ring into dialkylaminoalkylaryl-(aralkyl)-amine by reacting it with 2-bromethiazole, or by substitution of the hydrogen atom in the aminic group by an alkylaminoalkyl group.

In the present work, synthesis of the thiazole derivatives of ethylene- and trimethylene-diamine has been accomplished in another manner, namely: the dialkylaminoalkyl-(aralkyl)-amine is converted into the dihydrochloride (I), which, upon treating with ammonium rhodanide in chlorobenzene, is converted into the hydrogen rhodanide salt of asymmetric N-aryl-N-[β-dialkylaminoalkyl-(aralkyl)]-thiourea (II), and upon action of the alkali solution on the salt, the free base (III) is separated, according to the scheme:



Upon interacting equimolecular quantities of the asymmetric N-aryl-N-(β-dialkylaminoalkyl)-thiourea with chloroacetone, cyclization occurs, as the result of which asymmetrically-substituted ethylene- and trimethylene-diamine with the thiazole ring are formed in good yields according to the scheme:



The necessary secondary dialkylaminoalkyl-(or aralkyl) amines used as the intermediate substances for these syntheses were obtained by condensation of aryl or aralkylamines with dialkylaminoalkylbromide (or chloride) in toluene or in alcoholic solution, in the presence of anhydrous potash, as described in the preceding work [1]. Data for the secondary amines obtained are given in Table 1.

Among them compound (III) is described in the literature, and its yield is indicated as 45% of the theoretical [2]; the author has obtained this compound in 63% yield. N,N-Dimethyl-N'-benzyltrimethylenediamine (VI) was obtained by condensation of γ-dimethylaminopropylamine with benzyl chloride in pyridine in a manner similar to that for N,N-dimethyl-N'-(p-methoxybenzyl)-trimethylenediamine described in the preceding work [1]. The dihydrochlorides of the indicated secondary amines resulted on treatment of a solution of the secondary amine in absolute alcohol with the calculated quantity of hydrogen chloride in ether.

Asymmetric derivatives of N-aryl-N-[β-dialkylaminoalkyl- (or aralkyl)]-thiourea are given in Table 2.

They are colorless crystals with melting points below 150°. Poorly soluble in water, readily so in propyl, butyl and isoamyl alcohols. Yields of the recrystallized compounds vary from 23 to 55%.

Asymmetrically-substituted derivatives of ethylene- and trimethylene-diamine, containing the thiazole ring, and resulting from cyclization of asymmetric N-aryl-N-(β-dialkylaminoalkyl)-thioureas with chloroacetone, are given in Table 3.

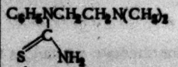
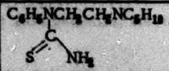
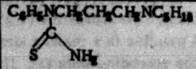
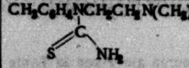
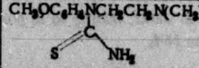
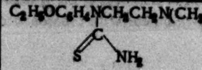
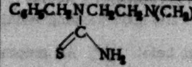
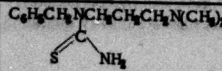
Preparations (XVI), (XVII), (XVIII), (XXII) and (XXIII) represent almost colorless viscous oily liquids with b.p. above 170° at 3 mm. After a certain length of time, they become yellow, and upon standing resinify.

Preparations (XV), (XIX), (XX) and (XXI) are crystalline compounds with m.p. below 100°. All preparations are soluble in organic solvents and do not dissolve in water. Almost all of them give well-formed picrates; exceptions are those compounds which contain the benzyl group. The dihydrochlorides are readily soluble in water. Some of them are very hygroscopic.

TABLE 1

Prep. No.	Structure	B.p.	Yield (%)	M.p. of dihydrochloride	M.p. of picrate	Empirical formula	Nitrogen (%)		Chlorine (%)	
							found	calc.	found	calc.
(I)	$C_6H_5NHCH_2CH_2NC_5H_{10}$	165-167° (4 mm)	76	174-175°	160°	$C_{25}H_{26}O_{14}N_8$ (dipicrate)	16.71	16.91	–	–
(II)	$C_6H_5NHCH_2CH_2CH_2NC_5H_{10}$ . . .	143-145° (3 mm)	80	228-229	–	$C_{14}H_{22}N_2 \cdot 2HCl$	9.76 9.82	9.62	24.12	24.17
(III)	p-$CH_3C_6H_4NHCH_2CH_2N(CH_3)_2$	120-123° (6 mm)	63	175-176	–	$C_{11}H_{18}N_2 \cdot 2HCl$	17.53 17.46	17.61	–	–
(IV)	p-$CH_3OC_6H_4NHCH_2CH_2N(CH_3)_2$	131-133° (4 mm)	66	165-166	–	$C_{11}H_{18}N_2O \cdot 2HCl$	10.65 10.69	10.48	–	–
(V)	p-$C_2H_5OC_6H_4NHCH_2CH_2N(CH_3)_2$	133-135° (4 mm)	65	160-161	–	$C_{12}H_{20}N_2O \cdot 2HCl$	9.85 10.03	9.96	24.97 25.26	25.02
(VI)	$C_6H_5CH_2NHCH_2CH_2CH_2N(CH_3)_2$	130-133° (6 mm)	53	207	–	$C_{12}H_{20}N_2 \cdot 2HCl$	10.33 10.28	10.56	26.47 26.40	26.78

TABLE 2

Prep. No.	Structure	M.p.	Yield (%)	Empirical formula	Nitrogen (%)		Sulfur (%)	
					Found	Calc.	Found	Calc.
(VII)	 $C_6H_5N(C(=S)NH_2)CH_2CH_2N(CH_3)_2$	131-132°	50	$C_{11}H_{17}N_3S$	18.72	18.83	14.49	14.35
(VIII)	 $C_6H_5N(C(=S)NH_2)CH_2CH_2NC_5H_{10}$	114-115	45	$C_{14}H_{21}N_3S$	15.82 15.68	15.96	12.36 12.27	12.16
(IX)	 $C_6H_5N(C(=S)NH_2)CH_2CH_2CH_2NC_5H_{10}$	112	40	$C_{15}H_{23}N_3S$	15.09 14.90	15.16	11.70 11.72	11.55
(X)	 $CH_3C_6H_4N(C(=S)NH_2)CH_2CH_2N(CH_3)_2$	130	52	$C_{12}H_{19}N_3S$	17.47 17.42	17.72	13.23	13.50
(XI)	 $CH_3OC_6H_4N(C(=S)NH_2)CH_2CH_2N(CH_3)_2$	146	50	$C_{12}H_{19}ON_3S$	16.49 16.37	16.60	12.92	12.64
(XII)	 $C_2H_5OC_6H_4N(C(=S)NH_2)CH_2CH_2N(CH_3)_2$	137-138	55	$C_{13}H_{21}ON_3S$	15.66 15.63	15.72	11.98 12.19	11.98
(XIII)	 $C_6H_5CH_2N(C(=S)NH_2)CH_2CH_2N(CH_3)_2$	105	38	$C_{12}H_{19}N_3S$	17.60 17.43	17.72	13.58 13.82	13.52
(XIV)	 $C_6H_5CH_2N(C(=S)NH_2)CH_2CH_2CH_2N(CH_3)_2$	102	23	$C_{13}H_{21}N_3S$	16.52 16.61	16.73	12.72 12.95	12.74

Preparation (XXI) resulted from the cyclization of N-(p-ethoxyphenyl)-N-(β-dimethylaminoethyl)-thiourea (XII) with bromoacetophenone. This preparation forms only the monohydrochloride and monohydrobromide. Both salts are very poorly soluble in water. Hence, replacement of the methyl group with the phenyl radical in position 4 of thiazole greatly decreases the solubility of these preparations in water.

The compounds listed in Table 3 were tested pharmacologically. It was found that they possess antihistaminic action, but antihistaminic activity below preparations of practical use.

EXPERIMENTAL

I. Synthesis of Asymmetric N-Aryl-(aralkyl)-N-(β-dialkylaminoalkyl)-thioureas.

As-N-phenyl-N-(β-dimethylaminoethyl)-thiourea (VII). A mixture of 42.6 g of the dihydrochloride of N,N-dimethyl-N'-phenylethylenediamine and 27 g of ammonium rhodanide in 100 ml of chlorobenzene was heated on a boiling water bath with mechanical stirring for 15 hours. The resulting yellow precipitate was filtered off, washed with a small quantity of ice water, and then dissolved in hot water. The solution was treated with activated carbon and filtered. From the filtrate there precipitated after a given length of time pretty white needles. The yield was 20.3 g — 50% of theoretical. The crystals, recrystallized from butyl alcohol, had a m.p. of 169-170° and gave a positive reaction for the rhodanide ion with a solution of iron chloride.

An analysis for nitrogen and sulfur confirmed the formation of the hydrorhodanide salt of asymmetrical thiourea, from which sodium carbonate does not liberate the free base.

Found %: N 19.92, 19.61; S 22.50, 22.62. $C_{12}H_{18}N_4S_2$. Calculated %: N 19.85; S 22.69.

The thiourea base resulted from a processing of the hydrorhodanide salt with 10% caustic soda solution. The base, recrystallized from butyl alcohol, melted at 131-132°.

The hydrochloride salt of thiourea resulted in quantitative yield on combining an ether solution of thiourea with an alcoholic solution of hydrogen chloride. M.p. of the hydrochloride salt was 199°.

Preparations (VIII)-(XIV) were obtained in a similar fashion.

As was to be expected, the secondary dialkylaminoalkylarylamines containing negative substituents in the para-position of the phenyl ring, and which formed only the monohydrochlorides (N,N-dimethyl-N'-(p-carbethoxyphenyl)-ethylenediamine and N-(β-piperidinoethyl)-p-bromoaniline [1]) did not form thiourea derivatives.

II. Synthesis of Thiazolylderivatives of Ethylene- and Trimethylenediamine.

N,N-Dimethyl-N'-phenyl-N'-2-(4-thiazolyl)-ethylenediamine (XV). 5 ml of chloroacetone (excess) was added to 4.6 g of as-N-phenyl-N-(β-dimethylaminoethyl)-thiourea (VII). After several minutes, a strong evolution of heat was observed, and the reaction mixture liquified. To complete reaction, the mixture was heated an additional hour on a water bath at 80-90°, was then dissolved in water, and the excess of chloroacetone was extracted with ether two times with 5 ml portions.

The aqueous solution was alkalized with caustic soda solution and was extracted three times with 10 ml portions of ether. The ether extract was dried with calcined potash, and after distilling off the ether, the remaining oil crystallized after a certain time. The crystals were dissolved in absolute ether, treated with activated carbon, filtered, and after evaporating the ether off, the remaining light-yellow crystals had a m.p. of 61-62°. Yield was 5.1 g.

If instead of the thiourea base, its hydrochloride or hydrorhodanide salt is used for condensation with chloroacetone, the same product in the same yield results.

The picrate was recrystallized from alcohol. M.p. 185°.

Found %: N 16.89, 17.07. $C_{19}H_{22}O_7N_6S$. Calculated %: N 17.14.

The dihydrochloride was obtained by addition of the calculated quantity of hydrogen chloride in ether solution to the basic solution in absolute alcohol.

Recrystallized from a mixture of absolute alcohol and ether. M.p. 192°. Readily soluble in water.

All preparations given in Table 3 were obtained similarly.

TABLE 3

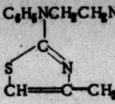
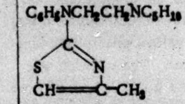
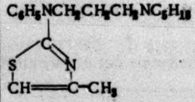
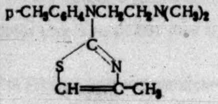
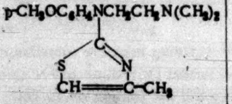
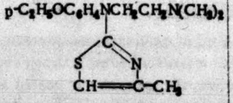
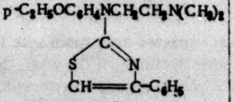
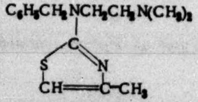
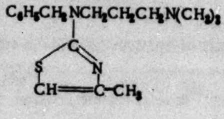
Prep. No.	Structure	Boiling point	Melting point	Yield (%)	M.p. of the dipicrate
(XV)	 $C_6H_5NCH_2CH_2N(CH_3)_2$ C S N CH C CH_3	–	61-62°	95	185°
(XVI)	 $C_6H_5NCH_2CH_2NC_5H_{10}$ C S N CH C CH_3	180-183° (4 mm)	–	76	179
(XVII)	 $C_6H_5NCH_2CH_2CH_2NC_5H_{10}$ C S N CH C CH_3	Not distilled	–	85	185
(XVIII)	 p-$CH_3C_6H_4NCH_2CH_2N(CH_3)_2$ C S N CH C CH_3	170-173° (4 mm)	–	84	189
(XIX)	 p-$CH_3OC_6H_4NCH_2CH_2N(CH_3)_2$ C S N CH C CH_3	–	47-48	91	201
(XX)	 p-$C_2H_5OC_6H_4NCH_2CH_2N(CH_3)_2$ C S N CH C CH_3	–	68.5	78	192 (with decomp.)
(XXI)	 p-$C_2H_5OC_6H_4NCH_2CH_2N(CH_3)_2$ C S N CH C C_6H_5	–	69	–	Monohydrobromide 213-215°
(XXII)	 $C_6H_5CH_2NCH_2CH_2N(CH_3)_2$ C S N CH C CH_3	171-174° (3 mm)	–	82	Perchlorate m.p. 144°
(XXIII)	 $C_6H_5CH_2NCH_2CH_2CH_2N(CH_3)_2$ C S N CH C CH_3	180-182° (3 mm)	–	84	177°

TABLE 3

M.p. of the dihydrochloride	Empirical formula	Nitrogen (%)		Sulfur (%)		Chlorine (%)	
		Found	Calculated	Found	Calculated	Found	Calculated
192°	$C_{14}H_{19}N_3S$	15.93 15.98	16.08	12.39 12.35	12.26	–	–
hygroscopic	$C_{29}H_{29}O_{14}N_9S$ (dipicrate)	16.76 16.61	16.62	4.52	4.21	–	–
164°	$C_{30}H_{31}O_{14}N_9S$ (dipicrate)	16.30 16.18	16.30	4.02 4.28	4.13	–	–
hygroscopic	$C_{27}H_{27}O_{14}N_9S$ (dipicrate)	17.32 17.41	17.19	4.37 4.46	4.36	–	–
144-145°	$C_{27}H_{27}O_{15}N_9S$ (dipicrate)	16.64 16.74	16.82	4.27	4.35	–	–
139-140° (with decomp.)	$C_{28}H_{29}O_{15}N_9S$ (dipicrate)	16.24 16.17	16.48	4.21 4.25	4.19	–	–
–	$C_{21}H_{25}ON_3S \cdot HBr$	9.16 9.23	9.37	7.36	7.14	Monohydrochloride 9.00 9.13	8.82
Identical with preparation (X) described in the preceding work [1].							
hygroscopic	$C_{28}H_{29}O_{14}N_9S$ (dipicrate)	16.71 16.66	16.85	4.24 4.21	4.28	–	–

Those preparations which did not crystallize after distilling off the ether (XVI, XVII, XVIII, XXII, XXIII) were redistilled in vacuo and identified in the form of the dipicrates.

N,N-Dimethyl-N'-benzyl-N'-2-(4-methylthiazolyl)-ethylenediamine (XXII) was obtained from the as-N-benzyl-N-(β-dimethylaminoethyl)-thiourea and chloroacetone, and after the usual treatment was redistilled in vacuo at 183-185° at 3 mm. The yield was 84% of theoretical. A light-yellow, viscous, oily liquid which formed the perchlorate upon treatment with a 30% solution of chloric acid. After recrystallization from alcohol, the perchlorate represented colorless needles with m.p. 144°. This perchlorate was found to be identical with the perchlorate obtained by the author upon treatment with chloric acid of the condensation product between 2-benzylamine-4-methylthiazole and dimethylaminoethylbromide in the presence of sodamide [1]. A mixed sample of the two perchlorates did not give depression.

The author duly acknowledges the valuable directions on the work by Professor A. I. Kiprianov, Active Member of the Ukrainian SSR Academy of Science.

SUMMARY

1. Eight asymmetrical N-aryl-(aralkyl)-N-(β-dialkylaminoalkyl)-thioureas have been obtained from the condensation of secondary dialkylaminoalkylaryl- (or aralkyl)amines with ammonium rhodanide.

2. Eight corresponding asymmetrically-substituted ethylene- and trimethylene-diamines, with the thiazole ring as substituent, have been isolated from condensation of the resulting asymmetric thioureas with chloroacetone.

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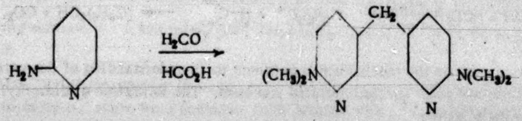
• See Consultants Bureau English translation, page 291.

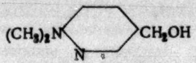
THE MECHANISM OF METHYLATION OF α-AMINOPYRIDINE ACCORDING TO LEUCKART, AND THE CONDENSATION OF DIMETHYLAMINOPYRIDINE WITH FORMALDEHYDE

A. I. Titov and A. N. Baryshnikova

In 1929 A. E. Chichibabin and I. L. Knunyants [1] discovered an interesting synthesis of tetramethyldiaminodipyridylmethane, heating α-aminopyridine with a mixture of formaldehyde and formic acid solution:



The authors studied the factors of dilution and of gradual addition of α-aminopyridine in the Chichibabin-Knunyants' reaction, in the hope of obtaining compounds with but one aminopyridine radical. The authors' assumption was found to be true – from the reaction product under the conditions given dimethylaminopyridine and the hitherto unknown 2-dimethylaminopyridine-5-carbinol were isolated:



Further experimental work allowed the assumption that the Chichibabin-Knunyants reaction starts with a rapid formation of condensation products between formaldehyde and the amino group of α-aminopyridine. Among them, the authors have succeeded in isolating for the first time in crystalline form methyl-di-(2-aminopyridine) $C_5H_4N{-}NH{-}CH_2{-}NH{-}C_5H_4N$. The remaining products of this reaction represent compounds of the same type $C_5H_4N{-}NH{-}CH_2OH$, $C_5H_4N{-}N{=}CH_2$ and its polymers, since upon their treatment with a mixture of dilute acids, they are easily restored to aminopyridine.

In addition, these products convert into methyl- and dimethylpyridine under the action of formic acid and the formate ion. An optimum acidity for the reaction exists – it does not proceed in a neutral medium or when considerable amounts of mineral acid are added.

Furthermore, dimethylaminopyridine condenses with formaldehyde to form dimethylaminopyridylcarbinol (I), and the latter with a second amine molecule to tetramethyldiaminodipyridylmethane (V). For both condensation reactions an optimum acidity was observed. From several indications (high polarity of the medium and of the reagents, catalysis by hydrogen ion, existence of an acidity optimum) it can be concluded that all of the transformations observed are of a complex ion character. The authors therefore considered that the following fundamental conditions for a complex ion process are realized in all of the transformations as formulated earlier by the authors [2]:

1) the appearance of opposite charges (+δ and −δ) of the directly interacting atoms, and the possibility for their increase at the expense of bond polarization;

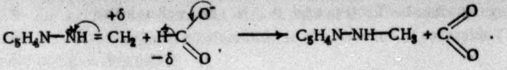
2) unsaturated coordination (spherical accessibility) for the directly reacting atoms.

In conformity with this postulate, and with the experimental data, the mechanism of formation of methyl- and of dimethyl-aminopyridine appears to the authors to be as follows. At first the attainment of reaction equilibrium is reached rapidly at the expense of interaction of the amino group with a proton and with formaldehyde, with resulting formation of the methylol bases, anil, dianil [methylene-di-(2-aminopyridine)] and methylenepyridylammonia, which do not require particular explanations:

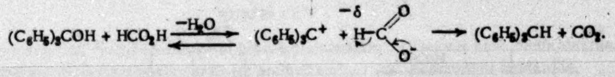
$$C_5H_4N{-}NH_2 + HCO_2^- H^+ \rightleftharpoons C_5H_4N{-}NH_3^+ + HCO_2^-,\ C_5H_4N{-}NH_2 + H_2C{=}O \rightleftharpoons C_5H_4NNH{-}CH_2OH \xrightarrow{-H_2O} C_5H_4N{-}N{=}CH_2.$$

$$C_5H_4N{-}N{=}CH_2 + C_5H_4N{-}NH_2 \rightleftharpoons C_5H_4N{-}NH{-}CH_2{-}NH{-}C_5H_4N,\ C_5H_4N{-}N{=}CH_2 + HCO_2^- H^+ \underset{}{\overset{-HCO_2^-}{\rightleftharpoons}} [C_5H_4NNH{=}CH_2]^+.$$

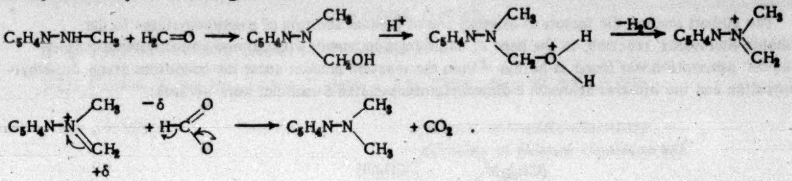
According to our concept and observations concerning the evolution of CO_2 in this reaction, the formation of methylaminopyridine should of course be accompanied by reduction of the methylenepyridylammonia cation by the formate ion:



Similar examples of the analogous action of formate ion are the reductions of mercury, silver, and finally triphenylcarbinol cations. The mechanism of the last process may be represented by the scheme:



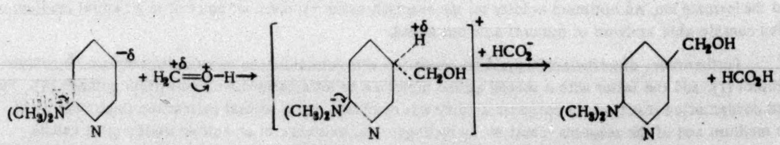
The development of a concept on the mechanism is pertinent to an understanding of the various modifications of the Leuckart reaction, and other similarly-related processes. The formation of dimethylaminopyridine will be presented by the following scheme:



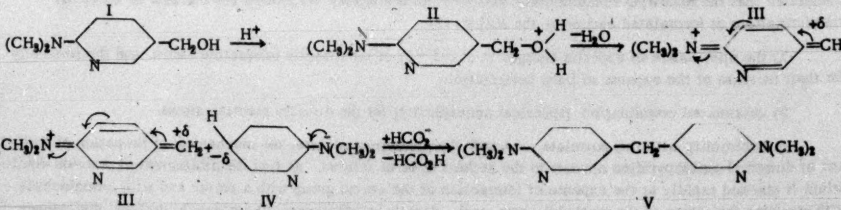
In contrast to the usual ionic reaction, the reduction of methyleneammonium cation by formate ion requires a corresponding orientation and activation energy for the ions.

For an understanding of the following condensation, it is important to mention that the optimum pH value also lies in the range of solution acidity given by formic acid-formate mixtures. This circumstance, together with the earlier-indicated conditions for reaction of the complex ion, leads to the following mechanism of formation of dimethylaminopyridylcarbinol:

$$[C_5H_4N(CH_3)_2H]^+ + HCO_2^- \rightleftharpoons C_5H_4N(CH_3)_2 + HCO_2H;\ H_2C{=}O + H^+ \rightleftharpoons [H_2C{=}O{-}H]^+.$$



The authors present the course of the second stage of the condensation in the following manner:



Dimethylaminopyridylcarbinol (I), along with the normal cation of the ammonium type, forms with the hydrogen ion an oxonium cation (II); the latter by splitting out water converts into the anhydro cation (III). Cation (III) (second line) reacts with free dimethylaminopyridine (IV), which leads to the formation of tetramethyldiaminodipyridylmethane (V); the splitting off of a proton from the transition complex (not shown in the scheme) occurs as in the preceding condensation, with formate anion participating.

In conformity with the understanding of the Chichibabin-Knunyants' reaction mechanism, by making use of added potassium formate, the authors succeeded in synthesizing tetramethyldiaminodipyridylmethane from aminopyridine in a very short time.

EXPERIMENTAL

Synthesis of Methylene-bis-(2-aminopyridine). a) 10 g of α-aminopyridine was dissolved in 20 ml of alcohol. 30 ml of formaldehyde was added to the solution rapidly, and then 40 ml of 40% NaOH. Heat was evolved. After cooling, it was extracted with ether and dried with potash. Upon slow evaporation of the ether, large colorless, prismatic crystals separated, with m.p. 120°. 7 g of pure product was isolated.

0.736 mg substance: 1.803 ml N_2 (23°, 745.6 mm). Found %: N 27.80. $C_{11}H_{12}N_4$. Calculated %: N 27.92.

The solubility of the product in water, even with heating, was very small; for its recrystallization, it is convenient to carry out same from acetone. Upon heating with dilute mineral acids, hydrolysis proceeded with separation of formaldehyde.

b) 10 g of α-aminopyridine and 3.5 g of paraform were heated in an open flask on a paraffin bath for 30 minutes at 120°, and for an additional 30 minutes at 150°. The loss in weight constituted 3.3 g. The residue in the flask crystallized from acetone, about 4 g of crystalline product resulting, which was identical with that described above.

Synthesis of Dimethyl-2-aminopyridine and Dimethyl-2-aminopyridyl-5-carbinol from 2-Aminopyridine. 150 ml of 20% formalin, turbid because of polymer content, and 50 ml of 90% formic acid were boiled to transparency and then 15 g of sodium formate was introduced. The solution of 3 g of α-aminopyridine in 10 ml of formic acid was boiled beforehand for 2 hours to make the formyl derivative, and was then added gradually, dropwise, to the mixture over a period of 3 hours, with reflux boiling. After the mixing, boiling was continued for an additional 3 hours. Then, to remove the possibility of further condensation reaction, 12 ml of concentrated sulfuric acid was added to the reaction mass, and the latter distilled on an oil bath until the temperature of the residue in the flask reached 120°. The residue in the flask was alkalized, and the bases were extracted with ether. The extraction was dried with potash and after the usual preliminary operations was fractionally distilled in vacuo (5 mm).

The following fractions resulted: I) 67-70° – 1.65 g; II) 140-160° – 1.06 g; III) 180-220° – 0.36 g.

The first fraction consisted principally of dimethylaminopyridine, as was established by determination of the boiling point, and by conversion into the picrate and into the nitro compound; they did not depress the melting point when heated with products of known structure.

The second fraction, boiling at about 155°, partially crystallized upon seeding with earlier-obtained dimethylaminopyridylcarbinol. After recrystallization from petroleum ether, the product was obtained as large crystals with m.p. 46°.

1.829 mg substance: 0.304 ml N_2 (27°, 732 mm). Found %: N 18.31. $C_8H_{12}ON_2$. Calculated %: N 18.43.

Small quantities of the carbinol can be separated and identified with the aid of the aurate, m.p. 146-147°.

2.346 mg substance: 0.1216 ml N_2 (24°, 729 mm). Found %: N 5.72. $C_8H_{13}ON_2Cl_4Au$. Calculated %: N 5.58.

The aurate of dimethylaminopyridine, which we have not described before, melts at 155-156°, and the tetramethyldiaminodipyridylmethane at 168-169°.

The chosen structure for dimethylaminopyridylcarbinol was proved by converting it into Chichibabin-Khunyants' tetramethyldiaminodipyridylmethane (experiment 3) by reaction with dimethylaminopyridine.

The third fraction also crystallized upon standing. After recrystallization from petroleum ether, there resulted a little of the pure tetramethyldiaminodipyridylmethane.

Condensation of Dimethylaminopyridylcarbinol with Dimethylaminopyridine. A mixture of 0.2 g of carbinol, 0.5. g of dimethylaminopyridine, 1 ml of 80% formic acid and 1 ml of water was heated for 10 hours at 100°. The reaction mass was evaporated on a water bath, and after alkalization, was redistilled with steam. The remaining oil (0.3 g) after seeding with tetramethyldiaminodipyridylmethane, crystallized. The melting point of the resulting product was 74-76°, and upon heating a mixed sample with known tetramethyldiaminodipyridylmethane an increase in m.p. to 78° was observed.

Under similar conditions a condensation product of carbinol with dimethylaniline was obtained, with a m.p. of 80°. Upon using hydrochloric acid instead of formic acid, condensation did not proceed.

Condensation of Dimethylaminopyridine with Formaldehyde.

Synthesis of Dimethylaminopyridylcarbinol. A mixture of 3 g of dimethylaminopyridine, 15 ml of 20% formaldehyde solution, 8 ml of formic acd and 3 ml of concentrated sulfuric acid was boiled for 19 hours on a reflux. 3.24 g of product resulted after alkalization, extraction with ether and distilling off the solvent from the extract. Redistillation at 5 mm pressure gave the following fractions: I 155-156°—1.23g; II 220-240°—1.22 g; the residue was 0.8 g.

The first fraction was very pure dimethylaminopyridylcarbinol, the second — tetramethyldiaminodipyridylmethane.

Synthesis of Tetramethyldiaminodipyridylmethane from Aminopyridine or Dimethylaminopyridine. A mixture of 3 g of aninopyridine, 8 ml of 90% formic acid, 15 ml of 20% formaldehyde solution and 6 g of potassium formate was boiled for 4 hours under a reflux condenser. The excess of formic acid and formalin was distilled off from the reaction mass on an oil bath until the temperature in the flask reached 150°. The residue in the flask was alkalized and extracted with ether:, the extract was dried with potash. 3.6 g of the product resulted from the ether extract after distillation, upon fractionation of this product at 6 mm pressure, the following distillates resulted: I 200-240° — 2.6 g; II 240-280° — 0.5 g.

The first fraction crystallized completely and consisted of quite pure tetramethyldiaminodipyridylmethane; the composition of the second fraction was not investigated. If 4 ml of concentrated sulfuric acid is added before distilling on an oil bath, small amounts of dimethylaminopyridine and carbinol will be found. Without adding formate, but adding sulfuric acid, before the beginning of the reaction, a large portion of aminopyridine remains without change.

With dimethylaminopyridine, carrying the reaction out under basic conditions, the yield and quality of product was increased.

SUMMARY

1. 2-Dimethylaminopyridine and 2-dimethylaminopyridyl-5-carbinol have been synthesized on the basis of reaction between 2-aminopyridine and formaldehyde in the presence of formic acid. A procedure for the rapid synthesis of bis-(2-dimethylaminopyridyl-5)-methane (tetramethyldiaminodipyridylmethane) according to the same method has been offered.

2. In the same manner, dimethylaminopyridylcarbinol and tetramethyldiaminodipyridylmethane have been synthesized from dimethylaminopyridine.

3. It has been demonstrated that acidity optima are evident for speed in methylation and condensation of the investigated reaction.

4. A mechanism of methylation of α-aminopyridine according to Leuckard, and of the condensation of dimethyl-aminopyridine with formaldehyde has been proposed and experimentally substantiated.

5. Two new compounds have been described: 2-dimethylaminopyridyl-5-carbinol and methylene-bis-(2-aminopyridine).

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[2] A. I. Titov, J. Gen. Chem. 16, 2011 (1946).

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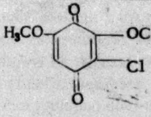
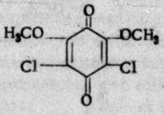
INVESTIGATIONS IN THE FIELD OF QUINONES

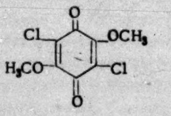
II. CHLORMETHOXYQUINONES

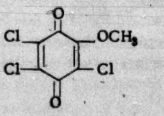
I. S. Ioffe and A. F. Sukhina

Quinone derivatives containing chlorine atoms and methoxyl groups have received but little study up to the present time. Only isolated representatives have been described. Thus, e.g., 3-chloro-2,6-dimethoxyquinone (I) was obtained [1] by passing chlorine through a solution of 2,6-dimethoxyquinone in chloroform. At the same time 3,5-dichloro-2,6-dimethoxyquinone (II) is also formed.


(I)

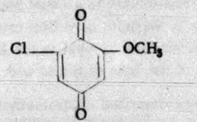

(II)

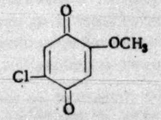

(III)


(IV)

3,5-Dichloro-2,6-dimethoxyquinone (II) is also formed [2] by treating chloroanil with methyl alcohol in the presence of caustic potash; however, with this reaction the main product is found to be 3,6-dichloro-2,5-dimethoxyquinone (III). The latter has also been obtained by methylation of chloroanilic acid with dimethylsulfate [3]. 3,5,6-Trichloro-2-methoxyquinone (IV) has been described, obtained from tetrachlorobenzene [4].

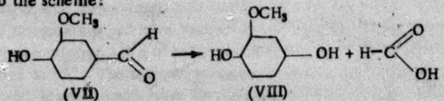
The simpler quinone derivatives which contain only one methoxyl group and one chlorine atom, in particular, 6-chloro-2-methoxyquinone (V) and 5-chloro-2-methoxyquinone (VI) as yet have not been described.


(V)

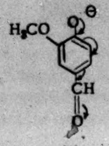

(VI)

The synthesis of these derivatives could be approached in a variety of ways, namely: methoxylation of chloroquinone, chlorination of methoxyquinone, and other means of synthesis from substances already containing chlorine atoms and methoxyl groups in definite positions. The authors synthesized chloromethoxyquinones (V) and (VI) starting with the isomeric chlorovanillins, and utilizing the Dakin reaction [5], which consists of treating o- or p-hydroxyaldehydes with hydrogen peroxide in alkaline solution. This reaction finally leads to breaking of the bond between the aromatic ring and the carbon atom of the aldehyde groups, which splits off as formic acid and is replaced by the hydroxyl group. Diatonic phenol which is produced can, by oxidation, be converted into the corresponding quinone derivative.

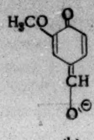
By such a reaction, 2-methoxyquinone, in particular, is formed. Here the initial substance is vanillin (VII), which upon treatment with hydrogen peroxide in alkaline solution is converted into 2-methoxyhydroquinone (VIII) according to the scheme:


(VII) (VIII)

Upon examination of this scheme the question arises as to why the bond between the carbon atoms of the benzene ring and the aldehyde group is so easily broken. It should be taken into account, however, that the Dakin reaction proceeds in alkaline medium, and that in such case, with the hydroxyaldehyde anion, e.g., of vanillin (a) there is displacement of electrons with replacement of the negative charge of the oxygen atom of the carbonyl group (b), with the appearance of the quinoid structure. A certain confirmation of this assumption is the fact that an alkaline solution of vanillin, and of other hydroxyaldehydes containing the hydroxyl groups in the o- or p- position to the carbonyl group, are colored yellow.



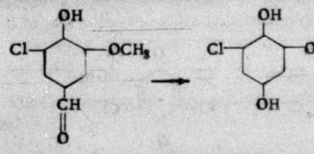
(a)



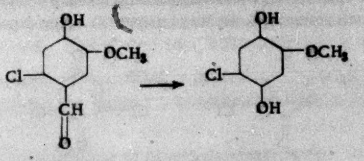
(b)

In such a quinoid state a double bond appears between the ring carbon atoms and the carbonyl group, which ruptures under the action of an oxidizing agent.

The isomeric chlorovanillins (IX) and (X) were subjected to the Dakin reaction. 3-Chloro-4-hydroxy-5-methoxybenzaldehyde (IX) resulted from direct chlorination of vanillin in chloroform [6], and separated in the form of colorless needles with m.p. 165°. Upon treating this compound with hydrogen peroxide, in alkaline solution, the authors obtained 6-chloro-2-methoxyhydroquinone (XI), from which, by oxidation, 6-chloro-2-methoxyquinone (V) resulted:



(IX) (XI)



(X) (XII)

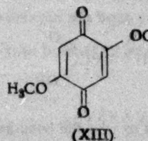
The authors obtained 2-chloro-4-hydroxy-5-methoxybenzaldehyde (X) by chlorination of acetyl vanillin [6], where, because of the hydroxyl group blocking, the chlorine atom entered the ring under the orienting influence of the methoxy group already in the para position to it. After saponification of the acetoxy group, 2-chloro-4-hydroxy-5-methoxybenzaldehyde resulted in the form of colorless crystals, with m.p. 168°. Upon treatment of this compound according to the Dakin reaction, 5-chloro-2-methoxyhydroquinone (XII) resulted, from which, by oxidation, the authors obtained 4-chloro-2-methoxyquinone (VI).

5-Chloro-2-methoxyquinone is somewhat less soluble in alcohol and in acetic acid than the 6-chloro-isomer. Both of the chloromethoxyquinones crystallize in the form of yellow crystals, distinct in their form and melting point. 6-Chloro-2-methoxyquinone crystallizes out from alcohol in the form of thin needle crystals with m.p. 159°; 5-chloro-2-methoxyquinone crystallizes out in the form of plates with m.p. 173°.

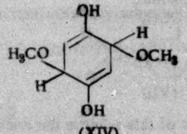
The authors also attempted synthesis of the above-described chloromethoxyquinone by methoxylating chloroquinone.

Direct introduction of the methoxyl group into the quinone ring was accomplished for the first time in 1901 by Bückel [7]. Upon heating benzoquinone in methyl alcohol in the presence of anhydrous zinc chloride, he obtained the dimethoxy derivative of quinone, which was identified with the oxidation product of 1,4-diamino-2,5-dimethoxybenzene. It was proved by the same fact that both methoxyl groups entered into the p-position to one another, with formation of 2,5-dimethoxyquinone (XIII).

The latter is obtained from this reaction in a yield of about 33% with regard to the quinone introduced into the reaction. However, this low yield corresponds to that theoretically calculated, it seems, because for each three quinone molecules introduced into reaction, only one can be converted to the 2,5-dimethoxyquinone, the two remaining ones serving to oxidize the primary addition product formed, of possible structure (XIV), transforming at the same time into hydroquinone.



(XIII)



(XIV)

The close-to-theoretical yield of 2,5-dimethoxyquinone is explained to a considerable extent by the fact that this compound is not very soluble in organic solvents, methyl alcohol in particular, and therefore, separating as it precipitates, does not decompose under the conditions which are relatively harsh for quinones.

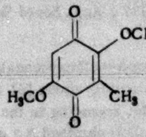
The authors attempted to increase the yield of 2,5-dimethoxyquinone by addition of oxidizing agents into the reaction medium, for example, anhydrous iron chloride or lead peroxide, but they were unsuccessful; it even led to a considerable lowering of the yield, which is evidently related to the action of the oxidizing agent upon the methyl alcohol.

The attempt to synthesize 2,5-dimethoxyquinone in high yield, using monomethoxyquinone prepared by the procedure given before, was unsuccessful [8]. Upon heating the latter with methyl alcohol in the presence of zinc chloride; only traces of 2,5-dimethoxyquinone were obtained. The principal product of the given reaction was found to be the dimer of methoxyquinone, blue-violet in color, and resulting from the action of acid reagents on methoxyquinone.

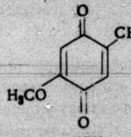
The formation of such a compound is characterized by coloration of the solution to an intense blue color, which can serve in particular as a qualitiative test for methoxyquinone.

These experiments are of value for a study of the methoxylation reaction mechanism. Up to this point, it seemed possible from these experiments that the synthesis of dimethoxyquinone was preceded by the formation of monoethoxyquinone with its subsequent methoxylation to 2,5-dimethoxyquinone. However, this hypothesis is contradicted by the fact that dimethoxyquinone is formed in good yield, corresponding to theory, and that upon obtaining dimethoxyquinone from quinone, the blue coloration which is characteristic for the dimerization product of monomethoxyquinone does not appear. It seemed more probable, therefore, that formation of 2,5-dimethoxyquinone is preceded by immediate addition of two molecules of methyl alcohol to the quinone molecule, with formation of addition product (XIV) which, upon oxidation, is converted into 2,5-dimethoxyquinone.

The Bückel reaction was also utilized in 1937 [9] for methoxylation of toluquinone. The authors of the work hoped to introduce into the latter molecule two methoxyl groups, with the formation of dimethoxytoluquinone (XV). However, they could only separate 2-methyl-5-methoxyquinone (XVI) – although in small yield.



(XV)



(XVI)

In the present article the authors have methoxylated chloroquinone under conditions of the Bückel reaction, hoping to obtain chloromethoxyquinone. However, the principal reaction product was found to be the 2,5-dimethoxyquinone, identified with the substance resulting directly from quinone. This indicates that under the relatively harsh Bückel reaction conditions heating chloroquinone with methyl alcohol in the presence of zinc chloride along with direct introduction of one methoxyl group into the quinone ring – substitution of chlorine by the second methoxyl group also takes place. Therefore, methoxylation of chloroquinone does not lead to the formation of chloromethoxyquinones.

EXPERIMENTAL

I. Methoxyquinone. 6 g of vanillin was dissolved in 40 ml of 4% caustic soda. To the light-yellow colored solution was added at once 40 ml of 5% hydrogen peroxide solution. Upon this, the solution gave off heat, up to 40°, and darkened. The dark-brown solution was left standing at room temperature for an hour. After 1 hour the solution was acidified with 20% sulfuric acid solution (8 ml), and was immediately placed in a cooling mixture. When the solution temperature had been lowered to −3°, it was added dropwise, with stirring, over a period of two hours, to the oxidizing mixture (40 g of sodium bichromate in 75 ml of 20% sulfuric acid). The oxidizing mixture should be pre-cooled to −5°. The mixture temperature should not exceed 0° during the oxidation. A temperature increase, even to +5°, lowers considerably the yield of methoxyquinone. For this reason it is not recommended that the experiment be carried out under laboratory conditions with large quantities of vanillin, since it is difficult to regulate the reaction temperature.

The methoxyquinone precipitated gradually in the form of fine yellow needles. After completion of the oxidation, the mixture with methoxyquinone precipitate was left standing for 2 hours at 0°, and the precipitate was then filtered off, washed with iced water and dried in a desiccator over calcium chloride. The weight of dry methoxyquinone was 3.4 g. The filtrate was treated several times with ether, the ether distilled off on a water bath, and upon separating of the crystals, the residue was poured into a Petri dish. The weight of dry residue was 0.5 g. The total weight of methoxyquinone was 3.9 g, i.e., 71% of the theoretical, calculating on vanillin. After recrystallizing from alcohol – light-yellow needle crystals, with m.p. 144°. Readily soluble in alcohol, ether, chloroform, glacial acetic acid and poorly soluble in water.

II. 6-Chloro-2-methoxyquinone. 3-Chloro-4-hydroxy-5-methoxybenzaldehyde resulted from the direct chlorination of vanillin in chloroform [6] and was separated in the form of colorless crystals with m.p. 165°.

6 g of 3-chloro-4-hydroxy-5-methoxybenzaldehyde was dissolved in 40 ml of 4% caustic soda. To the dark yellow colored solution, 40 ml of 5% hydrogen peroxide solution was added at once. The solution heated up to 40° and darkened. The dark brown solution was left standing for 30-40 minutes at room temperature. After 30 minutes, the solution was acidified with 20% sulfuric acid solution (8 ml) and placed in a cooling mixture. At this time 6-chloro-2-methoxyhydroquinone precipitated in the form of white needle crystals, with m.p. 140°. However, for the additional oxidation it is not necessary to separate the hydroquinone derivative. The viscous mixture can be immediately added to the oxidizing mixture of 40 g of sodium dichromate in 70 ml of 20% sulfuric acid, cooled to −5° for 2 hours. The temperature at this point should be strictly maintained as with the derivative of methoxyquinone.

The 6-chloro-2-methoxyquinone was precipitated in the form of fine light-orange crystals. After termination of the oxidation, the mixture was left to stand for 1-2 hours at −5°, the precipitate filtered off rapidly, washed with iced water and dried with calcium chloride. The weight of dry methoxychloroquinone was 4.28 g, i.e., 77% of the theoretical.

After crystallization from alcohol – light-orange crystals in the form of long, thin needles with m.p. 158-159°; readily soluble in alcohol, ether, chloroform, glacial acetic acid; poorly soluble in water.

0.1573, 0.1422 g substance: 0.1301, 0.1184 g AgCl. Found %: Cl 20.48, 20.75. $C_7H_5O_3Cl$. Calculated %: Cl 20.57. 0.1672, 0.1304 g substance: 0.2273, 0.1779 g AgI. Found %: OCH_3 17.95, 18.01. $C_6H_2O_2Cl\ (OCH_3)$. Calculated %: OCH_3 17.97.

III. 5-Chloro-2-methoxyquinone. 2-Chloro-4-hydroxy-5-methoxybenzaldehyde resulted from chlorination of acetylvanillin, followed by subsequent saponification of the acetoxy group [6]. 5-Chloro-2-methoxyquinone resulted from oxidation of 2-chloro-4-hydroxy-5-methoxybenzaldehyde, according to the method described for the methoxyquinone, with maintenance of the same conditions. The authors obtained 3.3 g of 5-chloro-2-methoxyquinone, i.e., 60% of the theoretical yield, from 6 g of 2-chloro-4-hydroxy-5-methoxybenzaldehyde.

After crystallization from alcohol – light yellow crystals in the form of platelets with m.p. 172-173°. Soluble in alcohol, ether, chloroform, acetone, benzene, glacial acetic acid to a lesser degree than the 6-isomer; poorly soluble in water.

0.1533, 0.1384 g substance: 0.1272, 0.1144 g AgCl. Found %: Cl 20.56, 20.67. $C_7H_5O_3Cl$. Calculated %: Cl 20.57, 0.1355, 0.1520 g substance: 0.1706, 0.2076 g AgI. Found %: (OCH_3) 18.10, 18.03. $C_6H_2O_2Cl\ (OCH_3)$. Calculated %: OCH_3 17.97.

SUMMARY

The synthesis of two new compounds, 6-chloro-2-methoxyquinone and 5-chloro-2-methoxyquinone, by treating the isomeric chloro-vanillins with hydrogen peroxide in alkaline solution, followed by oxidation of the resulting hydroquinone derivatives, has been described.

6-Chloro-2-methoxyquinone crystallizes in the form of thin, yellow needles, with m.p. 159°; 5-chloro-2-methoxyquinone crystallizes in the form of orange-yellow platelets, with m.p. 173°. 5-Chloro-2-methoxyquinone is soluble in organic solvents to a lesser extent than the 6-isomer.

It has been shown that upon methoxylating chloroquinone with methyl alcohol in the presence of zinc chloride, there occurs in addition to the direct introduction of the methoxyl group, a substitution of chlorine by a second methoxyl group, with the formation of 2,5-dimethoxyquinone which does not contain chlorine; therefore, direct methoxylation of chloroquinone cannot be used for the synthesis of chloromethoxyquinones.

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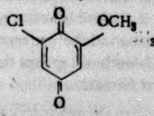
INVESTIGATIONS IN THE FIELD OF QUINONES

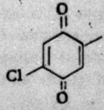
III. CHLORINATION OF METHOXYQUINONE

I. S. Ioffe and A. F. Sukhina

In the preceding article [1], derivation of 6-chloro-2-methoxyquinone (I) was described, as well as 5-chloro-2-methoxyquinone (II), starting with the isomeric chlorovanillins and unsuccessful attempts to synthesize chloromethoxyquinones by the methoxylation of chloroquinone.

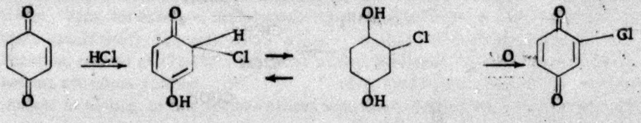


(I)



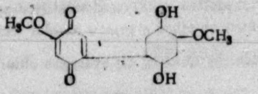
(II)

At the same time the authors studied the possibility of synthesizing these compounds by chlorination of methoxyquinone. The chlorination of quinones may be accomplished in two ways. One of them consists of treating quinone with anhydrous hydrogen chloride followed by oxidation of the addition product which is tautomeric with the chlorohydroquinone, to form the corresponding chloroquinone. Thus, in particular, the monochloroquinone [2] is obtained from benzoquinone according to the scheme:

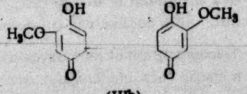


By the same procedure, a mixture of isomeric chlorotoluquinones [3] was obtained from toluquinone.

However, as investigations by the authors have shown, this method was found to be useless for synthesis of chloromethoxyquinones. Upon passing hydrogen chloride through a solution of the methoxyquinone in chloroform, a dark blue-violet precipitate separated which contained no chlorine, and after crystallization from nitrobenzene, melted at 238-240°. The same substance resulted upon addition of mineral acid to an acetate solution of methoxyquinone. It was found that this substance was identical with the already-described compound of the structure (IIIa) or (IIIb), obtained by oxidation of methoxyhydroquinone under specific conditions [4,5]:



(IIIa)



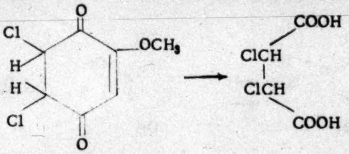
(IIIb)

From the above-stated, it follows that methoxyquinone, in distinction to benzoquinone and toluquinone, is dimerized to a two-ringed compound under the influence of the methoxyl group in the presence of mineral acids, and that the interaction with hydrogen chloride cannot, therefore, be utilized for derivation of chloromethoxyhydroquinone, nor chloromethoxyquinone from methoxy quinone, respectively.

The second method for synthesis of monochloroquinones is based upon the interaction of quinone with chlorine. From the addition product resulting at the same time – quinonedichloride – the corresponding monochloroquinone can be obtained by splitting off hydrogen chloride. However, this method, as our experiments have indicated, is not applicable to all cases, and the possibility of its utilization depends upon the properties and the stability of the resulting quinonedichloride. The simplest quinonedichloride, resulting from the addition of chlorine to benzoquinone, is very stable. It separates out in the form of colorless crystals, which melt sharply at 146° without decomposition. Nor does the colorless melt alter when heated to 160°. Only above 170-180° does the quinonedichloride slowly decompose with evolution of hydrogen chloride, but at this temperature the resulting monochloroquinone also breaks down. The toluquinonedichloride is somewhat less stable. It melts sharply at 135°, but the resulting melt at a temperature slightly higher than the melting point decomposes with the evolution of hydrogen chloride, and with formation of chlorotoluquinone. The methoxyquinonedichloride is even less stable. It begins to turn yellow above 100°, and at 120° melts with decomposition, evolving hydrogen chloride, with the formation of an orange melt, which, upon further heating, solidifies and again melts at 158-163°.

The above-indicated shows that the introduction of a methyl group, and to an even greater extent the methoxyl group, lowers the stability of the corresponding quinonedichlorides. It might be assumed that the quinonedichlorides resulting from interaction of chlorine with quinone derivatives would possess even less stability when containing several methyl or methoxyl groups. Indeed, when chlorine is passed through a solution of 2,6-dimethoxyquinone or 2,5-dimethylquinone in chloroform, under such conditions, when quinone, toluquinone or methoxyquinone is used, the corresponding dichlorides are obtained, 3-chloro-2,6-dimethoxyquinone [6] and 3-chloro-2,5-dimethylquinone [7] being obtained directly. It is possible under such conditions that the reaction proceeds by a preliminary addition of chlorine, with formation of the corresponding quinonedichlorides, but the latter are so unstable under the influence of 2-methyl or 2-methoxyl groups that they decompose with hydrogen chloride evolution, even at low temperature conditions of formation.

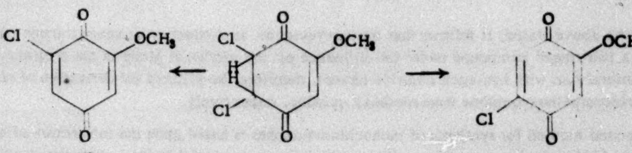
The comparatively low stability of methoxyquinonedichloride was utilized by the authors for a preparative synthesis of chloromethoxyquinones; at the same time, however, some unexpected results occurred. The methoxyquinonedichloride, itself, resulted [8] with comparative ease, on passing chlorine through a cooled solution of methoxyquinone in chloroform. Two chlorine atoms at the same time added to the double bond of that part of the quinone ring which was not connected with the methoxyl group. This was proved by the fact that upon oxidizing methoxyquinonedichloride, dichlorosuccinic acid resulted.



However, in the synthesis of methoxyquinonedichloride, there must be complete absence of even traces of hydrogen chloride in the chlorine which is passed through, which should be carefully checked, since the former promotes dimerization of the initial methoxyquinone into the above-indicated compound (III).

It was found that hydrogen chloride may also cause side reactions during the thermal decomposition of methoxyquinonedichloride; therefore, for the preparative synthesis of chloromethoxyquinone, the authors heated methoxyquinonedichloride under those conditions which promoted rapid elimination of hydrogen chloride from the reaction mixture. The authors placed a thin layer of methoxyquinonedichloride in a beaker, which was then placed in a thermostat heated to 125°. The product melted rapidly and solidified again in the form of a yellow-green crust. After cooling and powdering, the authors obtained a yellow powder which melted at 150-160°.

Decomposition of methoxyquinonedichloride, by splitting off hydrogen chloride, may lead to the formation of two isomeric chloromethoxyquinones:



(I)

(II)

Both of these chloromethoxyquinones were obtained by the authors [1] from the corresponding chlorovanillins. 6-Chloro-2-methoxyquinone crystallized out in the form of thin needles with m.p. 159°, and 5-chloro-2-methoxyquinone – in the form of platelets with m.p. 173°. The mixture of the two isomers begins to melt at approximately 130°.

The product obtained by the authors upon the thermal decomposition of methoxyquinonedichloride, melted sharply after crystallization from alcohol, at 173°. By analysis, by the properties, and by the mixing tests, it was identified with 5-chloro-2-methoxyquinone (II). The yield of this compound reached 70% of the theoretical. In the mother crystallization liquors the authors were unable to find the second isomer, 6-chloro-2-methoxyquinone (I). The absence of the latter is testified to by the fact that the crude, non-crystallized product of thermal decomposition of methoxyquinonedichloride melted at 160°, whereas a mixture of the two isomers begins to melt at a considerably lower temperature. The above-stated leads to the conclusion that the main product of thermal decomposition of methoxyquinonedichloride is 5-chloro-2-methoxyquinone.

Methoxyquinonedichloride is also unstable when heated in a number of solvents. The authors were convinced of this fact during attempts to crystallize the compound. Methoxyquinonedichloride solutions in alcohol in particular became yellow on heating and acquired an acid reaction as the result of hydrogen chloride evolution. The authors decided to use this observation for what seemed to be a more convenient preparative synthesis of chloromethoxyquinone. Indeed, upon introducing methoxyquinonedichloride into a boiling aqueous alcohol, with subsequent cooling of the solution, a yellow-colored crystalline precipitate separated out in a yield of about 60% of theoretical. However, this substance was found not to be 5-chloro-2-methoxyquinone. After crystallization, the resulting substance metled at 159°, and was identified with 6-chloro-2-methoxy-quinone (I).

Thus experiments have shown that upon decomposing methoxyquinonedichloride by splitting off hydrogen chloride, the direction of the reaction and the structure of the resulting chloromethoxyquinone depends upon the conditions of reaction. With thermal decomposition of methoxyquinonedichloride in the absence of solvent, the principal reaction product is found to be 5-chloro-2-methoxyquinone; upon heating with aqueous alcohol, the principal reaction product is found to be 6-chloro-2-methoxyquinone.

Further development of the work has demonstrated that thereaction direction also depends upon the character of the solvent. Thus, for example, upon introducing methoxyquinonedichloride into acetic acid heated to boiling, the solution immediately becomes yellow, and upon cooling, 5-chloro-2-methoxyquinone separates, which, after crystallization, melted at 172-173°. The same product will result when methoxyquinonedichloride is introduced into boiling anhydrous acetone. When methoxyquinonedichloride is introduced into 25% acetic acid heated to boiling, or into acetone diluted with water, 6-chloro-2-methoxyquinone results, m.p. 158-159°.

These experiments indicate that when methoxyquinonedichloride is heated in the absence of solvents, or in anhydrous solvents, hydrogen chloride cleavage proceeds in one specific direction, with the formation of 5-chloro-2-methoxyquinone; but upon heating in aqueous solvents, cleavage of hydrogen chloride proceeds in the other direction, with formation of 6-chloro-2-methoxyquinone. The same product will result when quinonedichloride is introduced into boiling water. Upon heating methoxyquinonedichloride in aromatic hydrocarbons, however, methoxyquinone is very stable. It does not decompose even upon one-hour boiling in xylene, which boils above the decomposition point of the crystalline methoxyquinonedichloride. By using benzene as the solvent, the authors were able to recrystallize methoxyquinonedichloride, thus obtaining it in the form of fine, almost colorless crystals, with decomposition point 120°. However, it was sufficient to add to the benzene only a few drops of water and the decomposition proceeded rapidly, with formation of 6-chloro-2-methoxyquinone.

SUMMARY

Upon passing hydrogen chloride through methoxyquinone solution in organic solvents, a dimerization product of methoxyquinone results immediately, precipitating in the form of a dark violet solid, melting at 238-240° after recrystallization from nitrobenzene, and is identical with that product described in the literature which is the oxidation product of methoxyhydroquinone. Therefore such a method cannot be used for the synthesis of chloromethoxyhydroquinone and, respectively, the chloromethoxyquinone by analogy with chlorohydroquinone.

For such purpose methoxyquinonedichloride can be used, which is obtained by passing chlorine through a solution of methoxyquinone in chloroform. In distinction to benzoquinonedichloride which boils sharply at 146°, and is stable to heat up to 160°, methoxyquinonedichloride when heated to 120° decomposes with evolution of hydrogen chloride and with conversion to 5-chloro-2-methoxyquinone.

Methoxyquinonedichloride is also unstable when heated in many organic solvents. Here the cleavage of hydrogen chloride, depending upon the character of the solvent, proceeds in two directions with the formation of two isomeric chloromethoxyquinones. Upon introducing methoxyquinonedichloride into anhydrous acetic acid or acetone, the same 5-chloro-2-methoxyquinone (m.p. 172-173°) is formed as that formed by melting crystals of methoxyquinonedichloride; however, in water, and also in aqueous acetic acid, acetone or alcohol, 6-chloro-2-methoxyquinone is formed (m.p. 159°).

Methoxyquinonedichloride is stable upon heating in benzene, toluene and xylene, and can be recrystallized from these solvents without decomposition.

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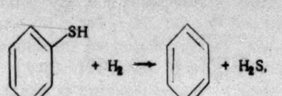
THE CATALYTIC TRANSFORMATION OF THIOPHENOL, DITHIORESORCINOL, THIANTHRENE AND DIPHENYLSULFIDE OVER ALUMINOSILICATE CATALYST

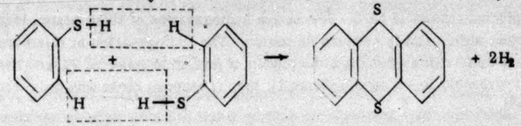
I. N. Tits-Skvortsova, A. I. Leonova, S. Ya. Levina and E. A. Karaseva

In the present work, data are given for the synthesis and catalytic transformation of sulfur compounds of the aromatic series, having as their composition divalent sulfur, namely: thiophenol, dithioresorcinol, thianthrene and diphenylsulfide. Synthesis of the aromatic sulfur compounds was carried out by procedures described in the literature. In some procedures slight modifications were introduced. To obtain comparative results, the investigated sulfur compounds were passed over aluminosilicate catalyst under standard conditions [1] adopted by the authors.

Thiophenol was taken as the simplest of the aromatic thiols, and was passed over aluminosilicate catalyst at 200°, 300° and 500°. In all of the experiments, benzene, thianthrene and the initial thiophenol were isolated from the catalyzate. The waste gases contained large amounts of hydrogen sulfide. Judging from the substances obtained, thiophenol on contact with catalyst undergoes transformation in two directions:



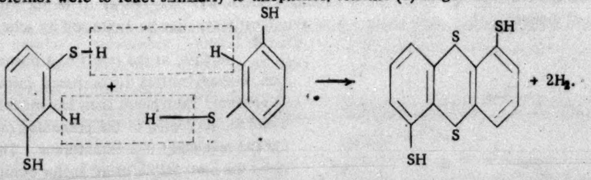
(1)



(2)

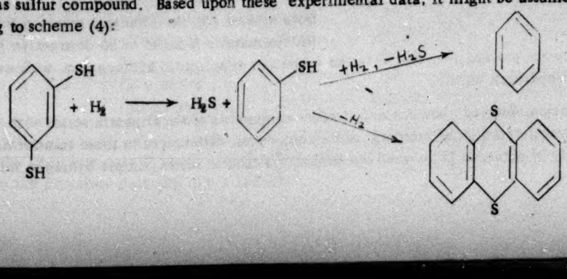
As the result of destructive hydrogenation, thiophenol is converted into benzene and hydrogen sulfide; dehydrogenation proceeds in a similar manner, leading to formation of two thiophenol molecules from the thianthrene molecule. Reaction (1) should be considered as the principal course of the reaction, since 4 times as much benzene is formed as thianthrene.

If dithioresorcinol were to react similarly to thiophenol, scheme (2) might take the following form:



(3)

It was of interest to clarify whether such a disulfhydryl derivative of thianthrene results from dithioresorcinol. The experiment with dithioresorcinol was carried out at 300°; benzene (23.8% of catalyzate weight) was separated from the resulting catalyzate, thiophenol (11.9%) and thianthrene (25.3%). About 50% of the sulfur that was contained in the initial dithioresorcinol was evolved in the form of hydrogen sulfide. The remaining sulfur was left in the catalyzate as sulfur compound. Based upon these experimental data, it might be assumed that the process proceeds according to scheme (4):

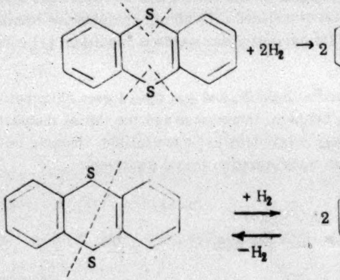


(4)

As the result of destructive hydrogenation, dithioresorcinol is converted into thiophenol. The latter, according to schemes(1 and 2) converts into benzene and thianthrene. Analysis of the waste gas after removal of hydrogen sulfide from it indicated the possibility of a hydrogenation reaction. The gas was composed chiefly of hydrogen and nitrogen. More complex compounds than thianthrene were not found in the catalysate; consequently, the reaction does not proceed according to scheme (3).

Since thianthrene was obtained from both thiophenol and from dithioresorcinol, it might be supposed that it is a stable compound. To verify this assumption, thianthrene was passed over aluminosilicate catalyst at 400°. Upon this it decomposed with evolution of hydrogen sulfide, but the decomposition was far from complete: unchanged thianthrene constituted about 45% of the catalyzate weight. The liquid portion of the catalyzate contained benzene (36% of the catalyzate weight) and traces of thiophenol.

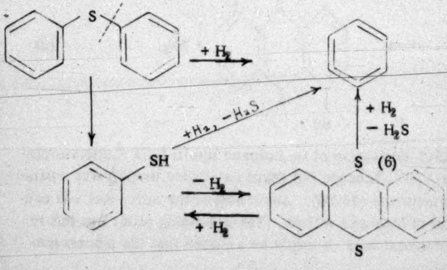
The decomposition of thianthrene can be shown according to the following scheme:



(5)

The fundamental process appears to be the destructive hydrogenation of thianthrene, leading to evolution of sulfur in the form of hydrogen sulfide, and to benzene formation. The hydrogenation of thianthrene to thiophenol evidently proceeds only to a small extent; but since the process is reversible (scheme 2), and the resulting thiophenol is further reduced irreversibly to benzene (scheme 1), then it becomes clear why only traces of thiophenol are present in the catalyzate.

For a study of the catalytic transformation of aromatic sulfides, the simplest of then was synthesized – diphenylsulfide, which was passed over aluminosilicate catalyst at 300, 350, 450 and 500°. From the catalyzates obtained, only two products were separated in all of the cases – benzene and thianthrene. The yield of benzene increased with increase in temperature, but the quantity of thianthrene decreased with increase in temperature. The reason is clear from the preceding: thianthrene itself converts into benzene at higher temperature. The catalyzates contained only traces of thiophenol. Evolution of hydrogen sulfide was observed at all temperatures investigated. Transformations of diphenylsulfide upon contact with aluminosilicate may be expressed by scheme (6).



(6)

At first, as the result of a destructive hydrogenation, diphenylsulfide decomposes, forming benzene and thiophenol. Thiophenol then irreversibly converts into benzene, according to the preceding (schemes 1, 2, and 5), and reversibly into thianthrene. Thianthrene is found to be the most stable of all sulfur compounds studied, but it also partially converts to benzene (scheme 5). The presence of thianthrene in the catalyzates indicates that its rate of formation is higher than its rate of decomposition. For thiophenol the correlation is in reverse: the catalyzate contains only traces of it. As can be seen from scheme (6), the principal reaction in all of these transformations is found to be destructive hydrogenation, and all of the processes proceed irreversibly to the formation of aromatic hydrocarbon, with evolution of the sulfur in the form of hydrogen sulfide.

If the transformations observed upon contact of sulfur compounds of the aliphatic series with aluminosilicate are compared with the transformations of aromatic sulfur compounds, differences in these transformations should be noted. Whereas a variety of reactions [2] is observed with the aliphatic series (simple hydrogen sulfide evolution, disproportionation of hydrogen, destructive hydrogenation), the main and most characteristic process in the aromatic series appears to be destructive hydrogenation, and the dehydrogenation reaction plays only a secondary role. The final products of transformation of sulfur compounds are also different: in the aliphatic series they are the alkenes, and in the aromatic series – the aromatic hydrocarbons. The common factor appears to be that the process in both the aliphatic and the aromatic series proceeds irreversibly toward the formation of hydrocarbons, and at the same time sulfur is evolved in the form of hydrogen sulfide.

EXPERIMENTAL

Sulfur compounds were passed over the catalyst under the following conditions: aluminosilicate catalyst in the amount of 30 g was placed in a reaction tube which was heated in an electric furnace. The experiment was carried out by a circulation method, passing the sulfur compounds over the catalyst in a weak stream of nitrogen (passage rate of the nitrogen was 600-800 ml per hour). The volumetric rate of flow of the substance was 0.25. In all cases of contact between the sulfur compounds and the catalyst, evolution of hydrogen sulfide was observed. The solid portion of catalyzate was filtered off and recrystallized from alcohol, the liquid portion washed with water until the hydrogen sulfide was removed, dried and fractionated to separate individual compounds from it. During fractionation there always resulted lower and higher fractions, which also indicated cracking and condensation reactions. Regeneration of catalyst was carried out after each experiment by letting in a stream of air at 500° up to the point of whitening of the catalyst, the air being removed from the reaction tube by nitrogen.

Thiophenol. Obtained by reduction of benzenesulfonyl chloride by two methods: a) using zinc dust as the reducing agent, b) using tin and hydrochloric acid as the reducing agent. Benzenesulfonyl chloride was obtained from benzene and chlorosulfonic acid [3] in 70% yield. 156 g of pure thiophenol was obtained from 320 g of benzenesulfonyl chloride by reduction with zinc and sulfuric acid [4]. The yield was 78.3% of the theoretical. B.p. was 68° (22 mm); n_D^{20} 1.5890; d_4^{20} 1.0787. The method of reducing benzenesulfonyl chloride by the use of tin and hydrochloric acid takes less time, is easy to carry out, but gives a lower yield of thiophenol and is economically inconvenient. 28 g of thiophenol (55% of the theroretical yield) was obtained from 80 g of benzenesulfonyl chloride. B.p 50.5-51.5° (7 mm); n_D^{22} 1.5883, d_4^{22} 1.0735.

Literature data: b.p. 71° (15 mm [4]); b.p. 77° (30 mm); $n_D^{23.2}$ 1.5861; $d_4^{23.2}$ 1.0739 [6].

The resulting thiophenol was passed over aluminosilicate catalyst under standardized conditions at 200, 300 and 500°. In all cases the catalyst obtained was a mixture of liquid and solid substances. After their separation, the liquid portion was fractionated. The solid substance separated from the higher fractions was combined with the solid substance from the catalyzate, the crystals were pressed out on a porous plate and crystallized from alcohol. The individual compounds resulting from the catalyzate, and their constants, are given in Table 1.

TABLE 1

Catalysis of Thiophenol at 200, 300 and 500°

temperature	thiophenol taken (g)	catalyzate obtained (g)	substances separated from catalyzate	quantity (g)	% yield of catalyzate weight	temperature		n_D^{20}
						boiling	melting	
200°	21.6	11.7	benzene	5.8	49.5	80.5-81°*	–	1.5004
			thianthrene	1.3	11.1	–	155° **	–
			thiophenol	0.9	7.7	164-166	–	1.5862
300	21.6	10.65	benzene	4.5	42.2	80-84	–	1.5020
			thianthrene	1.7	15.9	–	155	–
			thiophenol	0.7	6.6	165-166	–	1.5860
500	21.6	13.0	benzene	4.3	33.0	80-83	–	1.5018
			thianthrene	1.65	12.7	–	154	–
			thiophenol	1.9	14.6	165-166	–	1.5880
500	13.5	7.9	benzene	2.4	30.4	79-80	–	1.5002
			thianthrene	0.8	10.1	–	151	–
			thiophenol	1.4	17.7	164-166	–	1.5882

* According to the literature data [7] b.p. = 80.1°; n_D^{20} 1.5012.

** According to the literature data [8]: m p = 154-158°.

As can be seen from the data of Table 1, the principal substance resulting from the passage of thiophenol over the catalyst was found to be benzene. Thianthrene resulted at 200-300°, approximately four times less in amount than benzene.

The catalyzate obtained at these temperatures contained a small quantity of thiophenol. The presence of a large quantity (14.6%) of initial thiophenol in the catalyzate obtained at 500° created some doubt as to the activity of the catalyst. The catalyst was therefore regenerated for 10 hours at 500°. As can be seen from the data of the Table, the repeated experiment, carried out at 500°, confirmed the results of the preceding experiment.

The presence of a large amount of initial thiophenol in the catalyzate obtained at 500° may be explained by the fact that at this temperature all of the thiophenol is removed from the catalytic tube, while at 200 and 300° a portion of the thiophenol is retained. The fluctuations in thianthrene yields, however, are explained by unavoidable losses during its crystallization.

The total thianthrene obtained from the thiophenol was once more recrystallized from alcohol. Its melting point did not change and remained equal to 155°. It gave a characteristic blue coloration with concentrated sulfuric acid. A determination of C, H and S by the M. O. Korsun [9] method gave the following results:

6.840 mg substance: 16.700 mg CO_2; 2.280 mg H_2O; 6.035 mg SO_4. 6.120 mg substance: 14.949 mg CO_2; 2.020 mg H_2O; 5.420 mg SO_4. Found %: C 66.63, 66.57; H 3.73, 3.69; S 29.45, 29.56. $C_{12}H_8S_2$. Calculated %: C 66.61; H 3.73; S 29.66.

Dithioresorcinol was obtained by the method of Bourgeois [10]. This method, like that of the method for thiophenol synthesis, consisted of reducing m-benzenedisulfonylchloride with zinc dust and hydrochloric acid. The m-benzenedisulfonylchloride required for the reaction was obtained by the action of chlorosulfonic acid on benzene at high temperature.

To obtain m-benzenedisulfonylchloride, it was produced from benzene purified from thiophene by shaking with concentrated sulfuric acid. Sulfonation of the benzene was carried out in a round-bottomed flask, equipped with dropping funnel, reflux condenser and mechanical stirrer. 1950 g (16.8 moles) of chlorosulfonic acid was placed in the flask and 195 g (2.5 moles) of pure benzene added dropwise, with stirring, at room temperature. Reaction proceeded with the evolution of heat. The reaction mixture was then heated for 2 hours on an oil bath at 150-160°. After that the mixture was cooled to room temperature and was cautiously poured into a container filled with ice, with stirring. Strong heat evolution was observed here, and provision should be taken that there is always enough ice. At the end of the addition a brown-colored precipitate formed on the bottom of the container. The precipitate was filtered off and dried in air. The weight of crude product was 485 g (70.8% of the theoretical yield). To purify, the benzenedisulfonyl chloride was twice recrystallized from gasoline freshly distilled (b.p. 85-150°). 200 g (0.73 mole) of m-benzenedisulfonyl chloride was obtained, which amounted to 29.2% of theory. Light-colored crystals with m.p. 61-61.5°.

Literature data: m.p. 63° [11].

The resulting m-benzenedisulfonyl chloride was reduced, without further purification, to thioresorcinol. For this purpose 180 g of zinc dust and 200 ml of water were placed in a round-bottomed, three-necked flask equipped with reflux condenser and mechanical stirrer. The mixture was heated to 50° on a water bath, and 75 g (0.27 mole) of the m-benzenedisulfonyl chloride was added with stirring through the third neck of the flask. 20 g more of zinc dust was then added and the mixture heated on a water bath for 10 minutes at 70°.

The flask contents were cooled to 20°, and this temperature was maintained until a precipitate formed on the bottom of the flask in the form of a paste, grayish in color. A dropping funnel was placed in the third neck of the flask, and 1 kilogram of hydrochloric acid (sp. gr. 1.18) diluted with 500 ml of water, was added slowly, with mixing. The reaction was violent, and the flask was cooled with water.

Another 25 g of zinc dust was added and stirred for 2 hours at 20°. A caked precipitate formed on the bottom of the flask, gray in color. The acid layer was poured off from the precipitate, the precipitate filtered off, transferred from the beaker and repeatedly extracted with ether until the ether extract gave a mercaptan reaction (doctor test). The filtrate resulting from filtration of the precipitate was extracted three times with ether. The ether extracts were combined and dried with magnesium sulfate. After distilling off the ether, the dithioresorcinol was twice distilled in vacuo. The yield was 29.5 g (77.7% of theoretical). B.p. 128-128.5° (16 mm); m.p. 26-26.5°.

Literature data: b.p. 132° (20 mm); m.p. 27° [10].

Catalytic Transformation of Dithioresorcinol. 29 g of dithioresorcinol was passed over freshly-regenerated aluminosilicate catalyst at 300° under standardized conditions. In order that it might be introduced into the oven in the liquid state, the dropping funnel was warmed gently. The reaction was accompanied by a copious evolution of hydrogen sulfide. The weight of resulting catalyzate (a mixture of the liquid and the solid substances) was 6.7 g, which constituted 23.1% of the weight of dithioresorcinol taken. The solid portion of the catalyzate was separated from the liquid. The liquid catalyzate was washed with water to remove hydrogen sulfide and repeatedly extracted with 20% aqueous solution of KOH to recover mercaptans from it. After removal of alkali by washing with water, and drying with calcium chloride, benzene was isolated from the catalyzate in the amount of 1.6 g (23.8% of the catalyzate weight), with a b.p. of 79-80° (754 mm); n_D^{20} 1.5000; d_4^{20} 0.8770.

The alkaline extractions containing mercaptan were decomposed with hydrochloric acid, the mercaptan extracted with ether, the ether extracts washed to remove acid, and dried with magnesium sulfate. After distilling off the ether, thiophenol resulted (0.8 g), 11.9% of the catalyzate weight. B.p. was 166-169° (754 mm); n_D^{20} 1.5870; d_4^{20} 1.0716.

Thianthrene in the amount of 1.7 g (25.3% of the catalyzate weight), with m.p. 155-156°, was separated from the solid phase of the catalyzate by pressing out on a porous plate and crystallizing from alcohol. A sample mixed with an analyzed sample preparation of thianthrene did not give depression.

Hydrogen sulfide evolving during the course of the reaction was trapped by plumbite. The weight of washed and dried PbS precipitate was 51 g, which corresponded to 7.25 g of hydrogen sulfide, or 6.83 g of sulfur (52.1% of the theoretically possible). The sulfur remaining in the catalyzate was in the form of sulfur compounds.

An analysis of the outgoing gases, from which hydrogen sulfide was removed, gave: CO_2 0.26%, O_2 1.8%, H_2 10.5%, no CO, 0.6% saturated, no unsaturated, the remaining – nitrogen. The presence of hydrogen and of gaseous hydrocarbons in the gases indicated a cracking reaction.

Catalytic Transformation of Thianthrene. 5 g of thianthrene with m.p. 155-156° was passed over freshly-regenerated aluminosilicate catalyst at 400°. For this purpose the thianthrene was placed in the cold portion of the catalyst tube which projected out from the furnace. Upon gradually pushing the tube into the furnace, the thianthrene melted and flowed into the tube. Evolution of hydrogen sulfide was observed. The weight of resulting catalyzate (a mixture of liquid and solid) was 1.1 g (22% of the thianthrene weight taken). 0.7 g of benzene with n_D^{20} 1.5090 was separated from the liquid portion of the catalyzate. After repeated distillation, the benzene weight was 0.4 g (36% of the catalyzate weight), n_D^{20} 1.5000; m.p. 4°.

After distilling off the benzene, there remained in the flask several drops of high-boiling liquid with the characteristic sharp odor of thiophenol and a crystalline substance which was pressed out and combined with the solid portion of catalyzate The solid substance, when recrystallized from alcohol, weighed 0.5 g (45% of the catalyzate weight) and melted at 155°. This was the initial, unchanged thianthrene.

Diphenylsulfide. This was obtained by the action of sulfur monochloride on benzene in the presence of aluminum chloride [12]. 177 g (2.3 moles) of benzene purified to remove thiophene was placed in a round-bottomed flask equipped with mechanical stirrer, dropping funnel and a reflux condenser, along with 91 g (0.69 mole) of finely-ground commercial aluminum chloride. 85 g (0.6 mole) of sulfur monochloride in 81.5 g (1.04 mole) of benzene was added to the reaction mixture with stirring. The reaction mixture temperature was 10-13°. The aluminum chloride gradually disappeared and a dark-brown complex was formed. The reaction mixture was then stirred for an hour without cooling, and 1.5 hours at 30-40°, to the cessation of hydrogen chloride evolution. The resulting complex was decomposed with water and poured slowly, with stirring, into a container with ice chips. Decomposition proceeded violently, the color of the liquid changing from black to light yellow. A large quantity of sulfur deposited on the bottom and walls of the container. The liquid was transferred to a separatory funnel and the upper benzene layer was separated from the lower aqueous layer. The benzene layer was filtered off and the benzene distilled off. The remaining oil was cooled to 0°, again filtered to remove sulfur, and dissolved in methyl alcohol. The resulting solution was stirred for 3 hours at 0° and filtered off from the sulfur. After distilling off the alcohol, the diphenylsulfide was redistilled in vacuo at 147° (7 mm). To obtain a colorless preparation, the resulting diphenylsulfide was twice redistilled in vacuo. Yield was 86 g (76.6% of theoretical). B.p. 162.5° (18 mm); n_D^{20} 1.6312; d_4^{20} 1.1100.

Literature data: b.p. 162-163° (18 mm)[12]; $d^{15.2}$ 1.1175 [13]; $n_D^{18.5}$ 1.635 [14].

The diphenylsulfide obtained was passed over aluminosilicate catalyst under standard conditions at 300, 350, 450 and 500°. In all cases evolution of hydrogen sulfide was observed.

The liquid portion of the catalyzate was fractionated. The solid portion was pressed out on a porous plate and crystallized from alcohol.

The individual compounds separated from the catalyzate, and their constants, are given in Table 2.

TABLE 2

Catalysis of Diphenylsulfide at 300, 350, 450 and 500°

temperature	diphenylsulfide taken (g)	catalyzate obtained (g)	substances separated from catalyzate	quantity (g)	% yield of catalyzate wt.	temperature		n_D^{20}
						boiling	melting	
300°	11	8.7	benzene	0.7	8.0	78-80°	5-6°	1.5030
			thianthrene	1.2	13.7	–	153	–
			diphenylsulfide	4.8	55.2	150-155 (12 mm)	–	1.6364
350	11	5.4	benzene	1.6	29.6	79-80	5.2-6	1.5020
			thianthrene	0.8	14.8	–	152.6	–
			diphenylsulfide	traces	–	–	–	1.6327
450	11	5.1	benzene	1.8	35.3	79-81	–	1.5018
			thianthrene	0.75	14.7	–	154	–
500	11	6.2	benzene	4.0	64.5	78-80	–	1.5012
			thianthrene	0.7	11.3	–	152	–

As can be seen from the data of Table 2, the same substances, namely, benzene and thianthrene, result from the catalytic transformation of diphenylsulfide carried out over a wide range of temperatures. The yield of benzene increases with increased temperature, and the quantity of thianthrene decreases with increase in temperature. The initial diphenylsulfide was found in considerable quantity only at 300°. At all indicated temperatures, the strong, characteristic odor of thiophenol was evident.

SUMMARY

1. Sulfur compounds of the aromatic series undergo the following transformations upon contact with aluminosilicate catalyst at 300-500°:

a) thiophenol, as the result of destructive hydrogenation, converts into benzene and hydrogen sulfide: the process does not go to completion; simultaneously, but to a lesser degree, the dehydrogenation reaction proceeds with formation of thianthrene;

b) dithioresorcinol, as the result of destructive hydrogenation, converts at first into thiophenol, which then transforms as indicated above;

c) thianthrene, as the result of destructive hydrogenation, converts partially into benzene and hydrogen sulfide;

d) diphenylsulfide gives at first benzene and thiophenol, and the latter then transforms, according to point "a" above.

2. A destructive hydrogenation reaction is the principal, most characteristic reaction when sulfur compounds come in contact with aluminosilicate catalyst. The final transformation products are found to be aromatic hydrocarbons, the sulfur evolving as hydrogen sulfide. The decomposition process of sulfur compounds does not go to completion because of the high stability of some of them (thiophenol, thianthrene).

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INVESTIGATION IN THE FIELD OF HETEROCYCLIC COMPOUNDS

I. SYNTHESIS OF (QUINOLYL-6)-ALKANOLAMINES

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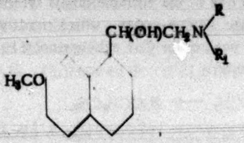
Aryl-β-aminoalkanols have been the objects of investigation for many years; the first stimulus to such work was the discovery of such interesting (in the pharmacological sense) natural compounds as adrenalin and ephedrine. The determinator of action of these compounds as pressor substances is conditioned by a characteristic side chain structure [1], having the character: $R_1CH(OH)\underset{\underset{R_2}{|}}{C}HNH_2$, where R_1 = an aromatic radical, R_2 = H or CH_3.

A great significance for the development of this work within the past few years is in connection with a concept expressed by Kaufman [2] back in 1913, to the effect that quinine in its structure may be considered to be an adrenalin-like substance, being a characteristic form of substituted aminoalkanol in the quinoline series, namely 4-(α-hydroxy-β-dialkylaminoalkyl)-6-methoxyquinoline. Proceeding from these premises, Kaufman [2] synthesized for the first time the simplest compound of this type, namely 4-(α-hydroxy-β-dialkylaminoethane)-6-methoxyquinoline:



where R and R_1 = H or CH_3.

It is of interest to note that this synthetic substance, constructed on the order of natural α-substituted aminoalkanols, possesses a pressor action similar to them. In order to more closely approximate the structure of these substituted β-aminoethanols to that of quinine, Kaufman and his co-workers [3] further synthesized a number of α-substituted β-aminoethanols, differing only in the nature of the β-substituted radicals on the nitrogen side chain. Recently, in connection with the development of an enormous amount of investigation directed toward the search for new antimalarial preparations, the aminoethanols of the quinoline series again attracted the attention of many chemists. From this viewpoint the works of Campbell and his group of co-workers [4,5] deserves mention. A majority of these investigations is devoted to synthesis of α-substituted β-aminoalkanols contained as the side chain in the 4- or 8 position of the quinoline ring. The exception is one work of the authors, who, on the assumption that 2-and 4-substituted quinolines are chemically similar, considered it worthwhile, for pharmacological research, to synthesize a derivative containing the alkanolamine side chain in the 2-position of the quinoline ring. The direction of these works is evidently conditioned first of all by the fact that up to the present time all of the known antimalarial preparations of the quinoline series — both natural and synthetic — are found to be 4- or 8-substituted quinolines. Furthermore, there are absolutely no works on such synthesis, so far as the authors are aware, of those substituted aminoalkanols in which the side chain is present in any other position (apart from the 8) of the benzene ring of the quinoline molecule. Synthesis of such a series of compounds undoubtedly offers considerable interest. The fact that the above-indicated α-(4-quinolyl)-β-aminoethanols of Kaufman (cited above), clearly possess vasoconstrictive action can be considered as an interesting case which confirms the position expressed by Barger [1] to the effect that in the character of this side chain is to be found one of the decisive factors determining manifestation of pressor action. But there are no data on the extent to which the position of this side chain in the quinoline ring influences the physiological action, inasmuch as no compounds of such type have been synthesized.

The present work, which is part of a designed, systematic research, has for its purpose the filling of this gap, and is devoted to the synthesis of related new derivatives of the quinoline series, namely: (6-quinolyl)-

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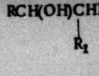
β-aminoethanol and (6-quinolyl)-β-aminopropanol, of the general formula:



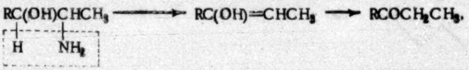
$$\underset{R_1}{RCH(OH)CHNH_2},$$

where R = the quinoline ring, R_1 = H or CH_3, $CH(OH)\overset{R_1}{C}HNH_2$ = side chain in position 6.

As the starting substance, the authors have taken 6-quinolylaldehyde, which has become a relatively accessible substance because of the work of M. A. Berkengeim and V. M. Rodionov [6]. By condensing it with the corresponding nitroalkanols in the presence of organic bases [7], the authors planned to obtain the substituted nitroalkanols, and by reduction (selective reduction of the nitro group) —the corresponding β-aminoalkanols. The authors carried out condensation of 6-quinolylaldehyde with nitromethane and nitroethane; condensation was carried out in alcoholic solution at ordinary temperature in the presence of diethylamine. The reaction proceeded very smoothly: by 24 hours the precipitation of well-formed slightly yellow crystals was observed, the quantity of which reached a maximum (about 80%) after 2-3 days. It is interesting to mention that the only reaction products were found to be the nitroalkanols, and in no case was it possible to determine the formation of unsaturated compounds.

Thus, in a respect, quinolylaldehyde parallels the properties of cinchonine aldehyde which, as was shown by Phillips [8], reacts with nitroalkane in an aldol-type condensation.

The second stage proceeds in a more complex manner, namely the synthesis of aminoalkanols. Although it was at once possible in the first orientation experiments to determine that reduction of the nitro group by hydrogen in the presence of Raney nickel catalyst proceeds quantitatively and selectively, judging from the quantity of hydrogen consumed, the yield of aminoethanols isolated in the form of hydrochloride salts was very low; and, moreover, it depended upon the amount of water in the medium in which reduction was carried out, fluctuating over a very wide range (27-73%). It was natural to assume that during the reprocessing of the reaction mixtures, the amino ethanols obtained by the authors, as with other compounds of this series, undergo hydraminic cleavage, transforming into quinoly ketone, which was also present in the yield of substances sought for. In fact, upon a careful investigation of the filtrate remaining after isolation of the hydrochloride salt of one of the aminoalkanols synthesized by the authors, it was possible to isolate a compound containing a functional ketone group, which readily gave a semicarbazone, and as analysis of the latter indicated, was found to be none other than ethylquinolyl ketone. The formation of this compound may be indicated by the following scheme:



where R = the quinoline ring.

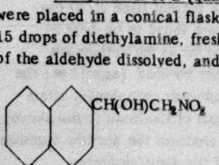
The authors further determined that this secondary ketone formation reaction is to a considerable degree dependent upon the amount of water in the alcohol in which reaction is carried out. The less water contained in the alcohol, the lower the ketone yield and the higher the aminoalkanol yield; fluctuating yields of the latter are therefore explained by this fact.

The resulting aminoalkanols were separated and characterized in the form of their hydrochloride salts.

EXPERIMENTAL

I. Synthesis of β-Nitroalkanols.

1. Synthesis of α-(quinolyl-6)-β-nitroethanol. 2.5 g of 6-quinolylaldehyde*, 30 ml of absolute ethyl alcohol were placed in a conical flask, and to the resulting suspension was added 3 ml of freshly-distilled nitromethane, and 15 drops of diethylamine, freshly distilled, was also added. Immediately upon introduction of the diethylamine all of the aldehyde dissolved, and the reaction mixture became slightly yellow. The flask was firmly stoppered with a cork and left to stand in a dark place at ordinary temperature for 48 hours. After 24 hours there appeared on the bottom of the flask a small quantity of cream-colored, well-formed, small crystals of the condensation product, and after 48 hours there was formed a copious, dense, cream-colored crystalline precipitate. It was filtered by suction and washed with a small quantity of cold alcohol; 2.15 g of substance resulted, constituting 67% of the theoretical yield: m.p. 137-138° (uncrystallized). After concentration of the filtrate and of the wash alcohol, it was possible to obtain a small quantity of crystals, but less pure. The resulting substance was readily soluble in hot alcohol, with greater difficulty in cold alcohol, and could be purified by crystallization from hot alcohol. A light, crystalline powder resulted, light-yellow in color, m.p. 139-140°.



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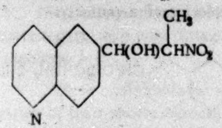
* Obtained from 6-methylquinoline by its oxidation with selenium dioxide according to the method of M.A. Berkengeim and V. M. Rodionov (cited above).

0.09850 g substance: 0.2185 g CO_2; 0.0407 g H_2O. 0.1004 g substance: 0.2224 g CO_2; 0.0425 g H_2O. 0.0987 g substance: 10 ml N_2 (18°, 758 mm). 0.0858 g substance: 9.95 ml N_2 (22°, 762 mm). Found %: C 60.40, 60.40; H 4.67, 4.70; N 12.92. 12.85. $C_{11}H_{10}O_3N_2$. Calculated %: C 60.55; H 4.58; N 12.84.

The substance dissolved readily in acids, forming salts. The hydrochloride salt was obtained for characterization. For this purpose, 1 g of pure nitroalkanol (m.p. 139-140°) was dissolved in 30 ml of alcohol, 2 ml of 1% alcoholic hydrogen chloride solution was added, and having added absolute ether to a dilute suspension of the reaction mixture, was left to stand for several hours. The crystals (needles) which precipitated out, consisting of the hydrochloride salt, were recrystallized from hot alcohol; the yield of pure product was 56%. The salt was readily soluble in water, forming a slightly yellow solution; it did not melt at 250°; it began to decompose upon heating above 250°.



0.1082 g substance: 4.27 ml 0.1 N $AgNO_3$. Found %: Cl 13.99 (Folgard). $C_{11}H_{10}O_3N_2 \cdot HCl$. Calculated %: Cl 13.80.

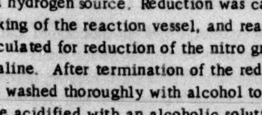
2. Synthesis of α-(quinolyl-6)-β-nitropropanol. 6-Quinolylaldehyde was condensed with nitroethane to obtain the derivative. 2.5 g of 6-quinolylaldehyde and 8 ml of absolute alcohol were introduced into a small conical flask; to the resulting suspension, 3.6 ml of freshly-distilled nitroethane and 15 drops of diethylamine also freshly distilled were added: complete dissolution of the aldehyde then occurred. The flask was stoppered firmly with a cork and left to stand at room temperature for 2 days. After this lapse of time, the precipitate was filtered by suction and washed with absolute alcohol. The alcohol was completely distilled off in vacuo from the filtrate. The precipitate, with the aid of a small quantity of alcohol, was transferred to the filter, filtered with suction, and washed with absolute alcohol. The combined precipitates were recrystallized from hot benzene. The total yield was 2.8 g, which constituted 77% of the theoretical yield: m.p. was 134°.

0.1234 g substance: 0.2802 g CO_2; 0.0580 g H_2O. 0.0976 g substance: 10.2 ml N_2 (23°, 758 mm). 0.1082 g substance: 12.0 ml N_2 (24.5°, 745 mm). Found %: C 61.97; H 5.22; N 12.02, 12.09. $C_{12}H_{12}O_3N_2$. Calculated %: C 62.07; H 5.17; N 12.07.

II. Synthesis of α-(Quinolyl-6)-β-aminoalkanols.

1. Synthesis of the Dihydrochloride of α-(quinolyl-6)-β-aminoethanol. 1 g of the above-obtained α-(quinolyl-6)-β-nitroethanol was dissolved with heating in 40 ml of absolute ethyl alcohol; the solution was transferred to a flask, stoppered firmly with a stopper equipped with two tubes; one was connected with a source of hydrogen, the other to a water pump. 5-10 g of Raney nickel catalyst was placed in the reaction flask, the former of which had been pre-washed with absolute alcohol to remove the water under which it is usually stored. Having removed all air from the apparatus as completely as possible with the aid of a water pump, the reaction flask was connected to a hydrogen source. Reduction was carried out under normal pressure and at standard temperature, with vigorous shaking of the reaction vessel, and reaction was terminated after 40 minutes, at which time the quantity of hydrogen calculated for reduction of the nitro group had been consumed, and the reaction mixture had become strongly alkaline. After termination of the reduction, the reaction mixture was filtered off from the catalyst; the latter was washed thoroughly with alcohol to the disappearance of alkaline reaction. The combined alcoholic filtrates were acidified with an alcoholic solution of hydrogen chloride and evaporated to dryness in vacuo. After distilling off the alcohol, a crystalline mass, yellow-brown or gray-green in color, remained (depending upon the standing time of the reaction mixture). After adding a few ml of absolute alcohol, the precipitate was transferred to a small Büchner funnel, carefully filtered by suction, washed with a small quantity of absolute alcohol and recrystallized from alcohol; the yield of crude product was 70-75%: yield of pure product was 35-40%.

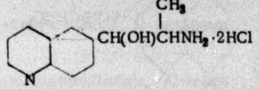
The dihydrochloride was recrystallized from alcohol as a fine, crystalline powder, readily soluble in water; it did not melt up to 250°, above which temperature it became black and decomposed.



0.1125 g substance: 0.2082 g CO_2; 0.0540 g H_2O. 0.1056 g substance: 9.75 ml N_2 (24°, 760 mm). 0.03740 g substance: 2.85 ml 0.1 N. $AgNO_3$. Found %: C 50.45; H 5.33; N 10.67; Cl 27.12 (Folgard); $C_{11}H_{12}ON_2 \cdot 2HCl$. Calculated %: C 50.60; H 5.36; N 10.73; Cl 27.18.

2. Synthesis of the dihydrochloride of α-(quinolyl-6)-β-aminopropanol. **Reduction of the above-described α-(quinolyl-6)-β-nitropropanol, as well as treatment of the reaction mixture, was carried out under the same conditions as indicated above for its lower homolog. After distilling off the ether, a yellowish-brown mass remained, which crystallized out as a grayish-green, crystalline precipitate upon standing. To separate the dihydrochloride, after distilling off the alcohol, several ml of absolute alcohol was added to the residue, the precipitate transferred to a small Büchner funnel and thoroughly washed with a small quantity of absolute alcohol. The yield of uncrystallized product fluctuated within a wide range (from 23-25%) in the case of high-colored residues after distilling off the ether, to 60-63%, in the case of gray.) To explain these fluctuations, both the crystalline reaction product and the filtrate remaining after isolation were investigated.**

a) For an investigation of the precipitate it was carefully crystallized from alcohol; in this manner white crystals resulted (needles), readily soluble in water, and insoluble in the usual organic solvents (with the exception of hot alcohol). As analysis indicated, these crystals were the dihydrochloride of α-(quinolyl-6)-β-aminopropanol.



0.1244 g substance.: 0.2385 g CO_2; 0.0654 g H_2O. 0.1178 g substance: 10.25 ml N_2 (19°, 758 mm). 0.0566 g substance: 4.1 ml 0.1 N $AgNO_3$; Found %: C 52.29; H 5.84; N 10.13; Cl 25.62. $C_{12}H_{14}ON_2 \cdot 2HCl$. Calculated %: C 52.38; H 5.82; N 10.18; Cl 25.74.

b) An investigation of the filtrate was carried out by means of its extraction several times with ether; for this purpose the filtrate was saturated first with sodium acetate, after which an oil separated, which was extracted with ether. The ether extract was dried with freshly-heated sodium sulfate, and the ether distilled off; after distilling off the ether, the residue was dissolved in alcohol and treated with the corresponding quantity of a semicarbazide hydrochloride and sodium acetate, and left to stand overnight. **The precipitate separated on the second day, was filtered off, and recrystallized from alcohol. White crystals with a yellowish shade, m.p. 218-220° As analysis showed, the crystals obtained were found to be the semicarbazone of α-(quinolyl-6)-β-ethyl ketone.**

3.105 g substance: 0.657 ml N_2 (24°, 724.5 mm). 3.215 g substance: 0.684 ml N_2 (25°, 723.5 mm). Found %: N 23.19, 23.10. $C_{13}H_{14}ON_4$. Calculated %: N 23.14.

SUMMARY

1. The condensation reaction of 6-quinolyladehyde with nitroalkanes has been studied. It has been established that condensation proceeds according to the aldol type, with formation of the corresponding nitroalkanols.

2. The catalytic reduction reaction of α-(quinolyl-6)-β-nitroalkanols in the presence of Raney nickel has been studied. It has been determined that at normal pressure and atmosphere the reduction proceeds selectively, affecting only the nitro group, with formation of the corresponding β-aminoalkanols. It has been determined that while treating the reaction mixtures obtained after reduction, the β-aminoalkanols formed undergo hydramine cleavage, transforming into the corresponding ketones, identified as the semicarbazones.

3. Two new α-substituted β-aminoalkanols have been synthesized: α-(quinolyl-6)-β-aminoethanol and α-(quinolyl-6)-β-aminopropanol.

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SYNTHESIS OF 3-ALKYLCHOLESTADIENES

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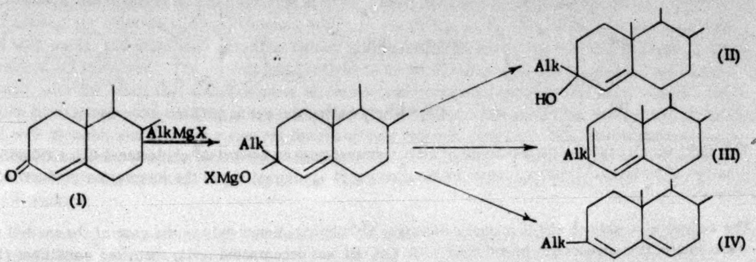
In spite of the considerable number of presently known dienes of the cholesterol series, of the substituted cholestadienes only two compounds are known – 3-chloro-$\Delta^{3,5}$-cholestadiene [1] and 3-phenyl-$\Delta^{3,5}$-cholestadiene [2]. The first was obtained by treatment of cholestenone with thionyl chloride, and the second, by interaction of cholestenone with phenylmagnesiumbromide, followed by decomposition of the Grignard complex with dilute hydrochloric acid.

Since cholestadienes with substituents in position 3 were of interest to the authors from the view of investigation of their photochemical transformations [3], the authors have used the latter method for the synthesis of various 3-alkylcholestadienes. The authors have investigated both conditions for the course of the Grignard reaction between cholestenone (I) and the various alkylmagnesium halides, the method of decomposing the resulting Grignard complex. All possible directions for this reaction can be shown by the following scheme:



As the authors' investigations have shown, the best conditions for reaction are found to be the addition, in ether solution, of a deficit amount of cholestenone (I) to the corresponding Grignard reagent with cooling and stirring. Depending upon conditions for the decomposition of the resulting Grignard complex, the authors were able to obtain both 3-alkyl-Δ^{4}-cholesten-3-ols (II) and various 3-alkyl-$\Delta^{2,4}$-cholestadienes (III), as well as 3-alkyl-$\Delta^{3,5}$-cholestadienes (IV).

Upon decomposing the Grignard complex with dilute hydrochloric acid, or acetic acid, there resulted as the principal product 3-alkyl-$\Delta^{3,5}$-cholestadienes (IV). The authors thus obtained 3-methyl-, 3-ethyl-, 3-n-butyl-, 3-cyclohexyl- and 3-hexyl-$\Delta^{3,5}$-cholestadienes.

All of these dienes exhibit a strong rotation to the left, do not give normal addition products with maleic anhydride, are not reduced by sodium in amyl alcohol, and possess a maximum absorption below 250 mμ. All of these properties confirm the structure as 3-alkyl-$\Delta^{3,5}$-cholestadienes [4].

A summary of the 3-alkyl substitutes of $\Delta^{3,5}$-cholestadiene, and their physical properties, is given in the Table.

name	melting point	$[\alpha]_D$	yield (%)
3-methyl-$\Delta^{3,5}$-cholestadiene	81.5-82°	−129°	73.7
3-ethyl-$\Delta^{3,5}$-cholestadiene	77-78	−120	68.0
3-n-butyl-$\Delta^{3,5}$-cholestadiene	64-65	−109.9	51.8
3-hexyl-$\Delta^{3,5}$-cholestadiene	46-48	− 93.8	40.0
3-cyclohexyl-$\Delta^{3,5}$-cholestadiene	144-146	− 84.6	50.0

The direct formation of 3-alkyl-$\Delta^{3,5}$-cholestadienes under the conditions of acid decomposition of the Grignard complex may be explained by the possibility of ease in allyl rearrangement of the 3-alkyl-Δ^{4}-cholesten-3-ol (II) which first forms, with its subsequent dehydration according to the scheme:

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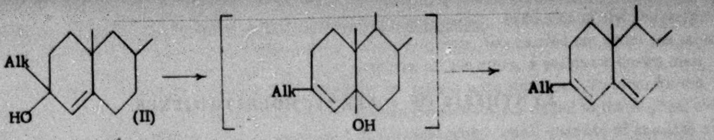
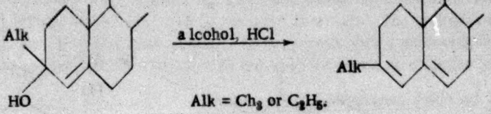


The presence of such rearrangement identical with transformation of the allo- and epiallo-cholesterins [5] was experimentally confirmed by the authors.

If decomposition of the Grignard complex which results from the interaction of cholestenone with the alkylmagnesium halide is carried out under very mild conditions, with the calculated quantity of ammonium chloride, strong cooling and stirring, then in the case of CH_3MgI and C_2H_5MgBr it is possible to obtain from the reaction products 3-methyl-Δ^4-cholesten-3-ol (II, Alk = CH_3) and 3-ethyl-Δ^4-cholesten-3-ol (II Alk = C_2H_5) in yield up to 80%, together with some quantity of uncrystallizable substance. The 3-alkyl-Δ^4-cholesten-3-ols thus obtained are found to be readily-crystallizable individual substances possessing a strong rotation to the right, which corresponds to a double bond position at C_4 [4]. Such carbinols are found to be extremely unstable compounds, as the result of which their isolation and crystallization require the maintenance of a series of precautions (see Experimental). Upon treating alcoholic solutions of the carbinols with hydrogen chloride in the cold, they are quantitatively decomposed to the corresponding 3-alkyl-$\Delta^{3,5}$-cholestadienes which are identical with those resulting from direct acid decomposition:



Alk = CH_3 or C_2H_5.

This fact, which confirms the existence of allyl rearrangement in 3-alkyl-Δ^4-cholesten-3-ols, explains the direct formation of 3-alkyl-$\Delta^{3,5}$-cholestadienes by the direct acid decomposition of the interaction products of cholestenone with AlkMgX.

The authors were able to effect synthesis of 3-alkyl $\Delta^{2,4}$-cholestadienes only in the case of the methyl derivative. If the interaction product of cholestenone with CH_3MgI was decomposed under specified conditions (NH_4Cl solution without cooling), it was then possible to isolate a crystalline substance with m.p. 68-69°, $[\alpha]_D$ −12.8°, which, by analysis, corresponded to 3-methylcholestadiene. This diene differed in its constants from the earlier obtained 3-methyl-$\Delta^{3,5}$-cholestadiene, and possessed an absorption in the range 260-280 mμ. When treated in alcoholic solution with hydrogen chloride, 3-methyl-$\Delta^{3,5}$-cholestadiene was formed in quantitative yield. These properties indicated that the 3-methylcholestadiene obtained, with m.p. 68-69°, and $[\alpha]_D$ −12.8° is 3-methyl-$\Delta^{2,4}$-cholestadiene (III Alk = CH_3).

An attempt to synthesize 3-methyl-$\Delta^{2,4}$-cholestadiene by direct dehydration of pure 3-methyl-Δ^4-cholesten-3-ol (sublimed in vacuo, redistilled with Al_2O_3, and so forth) did not lead to the desired results, since 3-methyl-$\Delta^{3,5}$-cholestadiene invariably resulted.

EXPERIMENTAL

I. Synthesis of 3-Alkyl-$\Delta^{3,5}$-Cholestadienes.

1. Synthesis of 3-methyl-$\Delta^{3,5}$-cholestadiene. 5.7 g of cholestenone solution in 36 ml of absolute ether was added dropwise over a period of 0.5 hour, with vigorous stirring, and at a temperature of −8°, to a solution of methylmagnesium iodide, prepared from 1.4 g of magnesium and 9.2 g of methyl iodide in 50 ml of absolute ether (5-fold excess). After addition of the cholestenone, the reaction mixture was stirred for 1 hour at 0°, and then slowly decomposed by the addition of 50 ml of 10% HCl, with stirring and ice cooling. The ether extract was separated, washed thoroughly with water, and dried with anhydrous sodium sulfate. After distilling the ether off in vacuo, a light yellow oil remained, which crystallized after the addition of a small quantity of alcohol. After recrystallizing three times from a mixture of alcohol and ether (2:1), 4.2 g of pure 3-methyl-$\Delta^{3,5}$-cholestadiene was obtained. White, lustrous needles with m.p. 81-82° and $[\alpha]^{14}_D$ −129° (144 mg of substance in 10 ml of CCl_4, α 1.87°). The yield was 73.7%, calculating on the basis of cholestenone taken for reaction. For analysis, the product was dried in vacuo at 40° over phosphoric anhydride.

6.085 mg substance: 19.669 mg CO_2; 6.638 mg H_2O. 0.1232 g substance: 0.3975 g CO_2; 0.1328 g H_2O.
Found %: C 88.21, 87.99; H 12.21, 11.97. $C_{28}H_{46}$. Calculated %: C 87.88; H 12.12.

3-Methyl-$\Delta^{3,5}$-cholestadiene does not give an addition reaction with maleic anhydride, nor is it reduced by sodium in amyl alcohol.

2. Synthesis of 3-Ethyl-$\Delta^{3,5}$-cholestadiene. 5.7 g of cholestenone in 36 ml of absolute ether was added to a four-fold excess of ethylmagnesium iodide solution (from 1.4 g of Mg and 7 g of C_2H_5I in 40 ml of absolute ether) over a period of 0.5 hour, with vigorous stirring and cooling to −8°. The reaction mass was then stirred for 1 hour at 0° and decomposed with 50 ml of a 10% solution of HCl. The ether extract was separated, washed thoroughly with water, and dried over anhydrous sodium sulfate. After distilling off the ether in vacuo, a light-yellow oil remained, which crystallized upon addition of a small quantity of alcohol. After recrystallizing 3 times from an alcohol-ether mixture (2:1), there resulted 4.0 g (68%) of 3-ethyl-$\Delta^{3,5}$-cholestadiene. Colorless, lustrous plates, with m.p. 77-78° and $[\alpha]_D^{17}$ −120.0° (100 mg of substance in 10 ml of CCl_4; α −1.2°). For analysis, the substance was dried in vacuo at 40° over phosphoric anhydride for 4 hours.

5.502 mg substance: 17.720 mg CO_2; 5.971 mg H_2O. 4.073 mg substance: 13.148 mg CO_2; 4.459 mg H_2O.
Found %: C 87.89, 88.09; H 12.14, 12.25. $C_{29}H_{48}$. Calculated %: C 87.80; H 12.20.

3. Synthesis of 3-n-Butyl-$\Delta^{3,5}$-cholestadiene. A double excess of butylmagnesium bromide (from 0.6 g of Mg and 3.6 g of n-butyl bromide in 40 ml of absolute ether) was added to a solution of 5 g of cholestenone in 35 ml of absolute ether over a period of 40 minutes with vigorous stirring and ice cooling. After completion of the addition, the reaction mixture was kept at 0° for 1 hour, and then decomposed by adding a solution of 10 g of ammonium chloride in 80 ml of water, with vigorous stirring at 0°. The ether layer was separated, washed with water, and dried with anhydrous sodium sulfate. After distilling the ether off in vacuo, a thick, light-colored oil remained. The product was dissolved in 20 ml of warm ethyl alcohol and 0.5 ml of conc. HCl was added, with the result that a light-colored oil immediately separated out from the warm solution, which gradually crystallized upon standing in the refrigerator (for 2-3 days). The crystalline product was filtered off, washed with alcohol, and dried in a vacuum desiccator over calcium chloride. After recrystallizing twice from alcohol and ether mixture (3:1), there resulted 3.0 g of 3-n-butyl-$\Delta^{3,5}$-cholestadiene, with m.p. 64-65°, and $[\alpha]_D^{14}$ −109.9° (233 mg substance in 10 mg CCl_4, α −2.6°). The yield constituted 51.8%, based upon cholestenone taken for reaction.

For analysis, the 3-n-butyl-$\Delta^{3,5}$-cholestadiene was dried in a vacuum desiccator over phosphoric anhydride.

3.674 mg substance: 11.842 mg CO_2; 4.059 mg H_2O. 0.0801 g substance: 0.2584 g CO_2; 0.0888 g H_2O.
Found %: C 87.95, 87.97; H 12.46, 12.32. $C_{31}H_{52}$. Calculated %: C 87.66; H 12.34.

4. Synthesis of 3-n-Hexyl-$\Delta^{3,5}$-cholestadiene. A double excess of hexylmagnesium bromide (from 0.63 g of Mg and 4.3 g of n-hexyl bromide in 35 ml of absolute ether) was added to a solution of 5 g of cholestenone in 35 ml of absolute ether, with vigorous stirring at 0°. After stirring for 1 hour at 0°, the reaction mixture was decomposed as before with ammonium chloride solution. The ether layer was separated, washed with water, dried over anhydrous sodium sulfate, and the ether distilled off in vacuo. The remaining viscous, colorless oil, which did not crystallize on standing, was dissolved in 30 ml of ethyl alcohol and 0.5 ml of concentrated HCl was added. The colorless oil which then separated out gradually crystallized upon prolonged standing in the refrigerator (10-12 days). The crystalline product was filtered off, washed with alcohol, and dried in a vacuum desiccator over calcium chloride. After double recrystallization from a small quantity of ethyl acetate, 2.3 g of pure 2-n-hexyl-$\Delta^{3,5}$-cholestadiene resulted with a constant m.p. of 46-48° and $[\alpha]_D^{18}$ −93.8° (252 mg substance in 10 ml CCl_4; α −2.5°). The yield was 40%, based on cholestenone.

For analysis, the diene was dried in a vacuum desiccator over phosphoric anhydride.

0.1042 g substance: 0.3344 g CO_2; 0.1202 g H_2O. 0.1026 g substance: 0.3288 g CO_2; 0.1160 g H_2O.
Found %: C 87.52, 87.40; H 12.78, 12.56. $C_{33}H_{56}$. Calculated %: C 87.54; H 12.46.

5. Synthesis of 3-Cyclohexyl-$\Delta^{3,5}$-cholestadiene. A solution of 5 g of cholestenone in 30 ml of absolute ether was added dropwise over a period of 0.5 hour to a solution of cyclohexylmagnesium bromide prepared from 0.83 g of Mg and 5.5 g of cyclohexylbromide in 50 ml of absolute ether, with vigorous stirring and cooling to 0° during the addition. The reaction mixture was stirred for 2 hours at 0°, and then decomposed at the same temperature with 10% HCl solution (50 ml). The ether layer was separated, washed with water, dried over

anhydrous Na_2SO_4, and the ether distilled off to a small volume. A small volume of absolute alcohol was added to the resulting crystalline precipitate, and the precipitate filtered off. After two recrystallizations from ethyl acetate or alcohol-benzene mixture (9:1), 3 g (50%) of 3-cyclohexyl-$\Delta^{3,5}$-cholestadiene was obtained, with m.p. 144-146° and $[\alpha]_D^{14}$ −84.3° (105 mg substance in 10 ml $CHCl_3$ α −0.94°).

For analysis, the diene was dried in vacuo at 60° over phosphoric anhydride.

0.1236 g substance: 0.3999 g CO_2; 0.1339 g H_2O. 0.1230 g substance: 0.3976 g CO_2; 0.1320 g H_2O. Found %: C 88.10, 88.16; H 12.22, 11.92. $C_{33}H_{54}$. Calculated %: C 87.92, 12.07.

II. Synthesis of 3-Alkyl-Δ^4-cholesten-3-ols and Their Conversions.

1. Synthesis of 3-Methyl-Δ^4-cholesten-3-ol. A solution of 5.7 g of cholestenone in 35 ml of absolute ether was added dropwise at −8°, with vigorous stirring, to a solution of methylmagnesium iodide prepared from 1.4 g of Mg and 9.2 g of CH_3I in 50 ml of absolute ether. After keeping at 0° for 0.5 hour, the reaction product was decomposed at −8 to −10° by the slow addition of a solution composed of 10 g of ammonium chloride in 100 ml of water, and stirred for 0.5 hour at room temperature. The ether was separated, washed with water, dried over anhydrous sulfate and the ether distilled off in vacuo. The residue was a crystalline substance, in the form of long thin needles and had an m.p. of 102-104°. The weight was 4.7 g, which constituted about 79.6% of the theoretical, calculating for the cholestenone taken into reaction. After two recrystallizations from alcohol-ether mixture (4:1), and then from a small volume of ether, 3.5 g of the substance with m.p. 112-114° resulted with $[\alpha]_D^{14}$ +60.9° (200 mg substance in 10 mg CCl_4, α +1.29°). The substance obtained is extremely unstable with respect to heat and to traces of acids, and so it is necessary during the crystallization process to avoid prolonged heating, and to the solvents should be added a small quantity (2-3 drops) of ammonium chloride solution.

For analysis, the substance was dried in a vacuum desiccator over calcium chloride.

4.417 mg substance: 13.301 mg CO_2; 4.758 mg H_2O. 0.1040 g substance: 0.3130 g CO_2; 0.1120 g H_2O. 0.1051 g substance: 0.3153 g CO_2; 0.1146 g H_2O. Found %: C 82.17, 82.08, 82.0; H 12.05, 11.96, 12.11. M 415.2, 403.8, 402.5 (Rast). $C_{28}H_{48}O \cdot {}^1/_2\ H_2O$. Calculated %: C 82.08; H 12.05; M 409.7.

2. Conversion of 3-Methyl-Δ^4-cholesten-3-ol to 3-Methyl-$\Delta^{3,5}$-cholestadiene. 5 drops of concentrated HCl was added to a solution of 2 g of 3-methyl-Δ^4-cholesten-3-ol in 150 ml of 96% ethyl alcohol, and the solution was boiled for 5 minutes. After cooling, the resulting precipitate was filtered off, washed with alcohol and dried, m.p. 77-79°. After recrystallization from alcohol-ether mixture (3:1), there resulted a substance in the form of lustrous needles, with m.p. 81.5-82° and $[\alpha]_D^{14}$ −129.8°, which did not give a melting point depression with the earlier obtained 3-methyl-$\Delta^{3,5}$-cholestadiene. Yield was 1.5 g (79.9 %).

3. Synthesis of 3-Ethyl-Δ^4-cholesten-3-ol. In a manner similar to the synthesis of 3-methyl-Δ^4-cholesten-3-ol, 4.8 g of crude 3-ethyl-Δ^4-cholesten-3-ol with m.p. 84-88° resulted from 5.7 g of cholestenone. After double recrystallization from ether by addition of a small volume of alcohol, 3.5 g of substance resulted, which crystallized in the form of long, thin needles, with a constant m.p. of 89-91° and $[\alpha]_D^{17}$ + 60.6° (165 mg substance in 10 ml CCl_4, α +1.0°). As with the methyl derivative, 3- ethyl-Δ^4-cholesten-3-ol is very unstable toward heat and to the presence of traces of acids.

For analysis, the substance was dried in a vacuum desiccator over calcium chloride.

4.528 mg substance: 13.675 mg CO_2; 4.925 mg H_2O. 0.1192 g substance: 0.3584 g CO_2; 0.1306 g H_2O. Found %: C 82.42, 82.00; H 12.17, 11.98. M 421.0, 419.5 (Rast). $C_{29}H_{50}O \cdot {}^1/_2\ H_2O$. Calculated %: C 82.27; H 12.06; M 423.7.

4. Conversion of 3-Ethyl-Δ^4-cholesten-3-ol into 3-Ethyl-$\Delta^{3,5}$-cholestadiene. 5 drops of conc. HCl was added to a solution of 1 g of 3-ethyl-Δ^4-cholesten-3-ol in 50 ml of 96 % ethyl alcohol, and the solution was boiled for 5 minutes. The crystalline product which resulted on cooling (lustrous crystals) was filtered off, washed and dried; m.p. 76-77°. After a single crystallization from an alcohol-ether mixture (3:1), 0.8 g of the substance resulted (88.8%), with m.p. 77-78° and $[\alpha]_D^{14}$ −119.1°, which did not give a melting point depression with the earlier-obtained 3-ethyl-$\Delta^{3,5}$-cholestadiene.

III. Synthesis of 3-Methyl-$\Delta^{2,4}$-cholestadiene and Its Conversion.

A solution of 11.4 g of cholestenone in 75 ml of ether was added, over a period of 45 minutes with vigorous stirring and cooling to −8°, to a solution of methylmagnesium iodide prepared from 2.8 g of Mg and 18.2 g of CH_3I in 100 ml of absolute ether. The reaction mass was stirred for 1 hour at 0°, and then slowly decomposed with stirring by the addition of a solution of 20 g of ammonium chloride in 180 ml of water, without cooling, and with rapid boiling of the ether. The ether layer was separated, using anhydrous sodium sulfate, and the ether was distilled off in vacuo. The remaining light-colored viscous oil gradually crystallized upon standing. The crystalline residue was recrystallized from an alcohol-ether mixture (3:1), and the substance was obtained in the form of white lustrous plates, with m.p. 65-67°. After three recrystallizations, 8.7 g (85.9 %) of pure 3-methyl-$\Delta^{2,4}$-cholestadiene resulted, with a constant m.p. of 68-69° and $[\alpha]_D^{18}$ $-12.5°$ (0.1437 g substance: 10 ml $CHCl_3$, α $-0.17°$).

For analysis, the product was dried in a vacuum desiccator over phosphoric anhydride.

3.946 mg substance: 12.766 mg CO_2; 4.271 mg H_2O. 4.953 mg substance: 15.996 mg CO_2; 5.341 mg H_2O. Found %: C 88.27, 88.13; H 12.11, 12.07. $C_{28}H_{46}$. Calculated %: C 87.88; H 12.12.

0.5 ml of conc. HCl was added to a solution of 1.4 g of 3-methyl-$\Delta^{2,4}$-cholestadiene in 200 ml of 96% ethyl alcohol and the solution was boiled for 5 minutes. The resulting lustrous white needles obtained on cooling were filtered off, washed with alcohol and dried. Weight was 1.3 g, m.p. 79-80°. After recrystallization from alcohol-ether mixture (3:1), 1.2 g of the substance with m.p. 81-82° and $[\alpha]_D^{18}$ $-129.3°$ resulted, which did not give depression in melting point with the earlier-obtained 3-methyl-$\Delta^{3,5}$-cholestadiene. The yield was quantitative.

SUMMARY

1. The Grignard reaction between certain AlkMgX compounds and Δ^4-cholestenone has been studied.

2. By means of direct acid decomposition of the interaction products from alkylmagnesium halides and the cholestenone, a series of 3-alkyl-$\Delta^{3,5}$-cholestadienes has been obtained.

3. Under specified conditions of decomposition of the Grignard complex, 3-methyl-Δ^4-cholesten-3-ol, 3-ethyl-Δ^4-cholesten-3-ol and 3-methyl-$\Delta^{2,4}$-cholestadiene have been obtained. It has been demonstrated that these compounds when treated with an alcoholic solution of hydrogen chloride, are able quantitatively to convert into the corresponding 3-alkyl-$\Delta^{3,5}$-cholestadienes.

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ABSORPTION SPECTRA AND STRUCTURES OF LOCAL-ANESTHETIC DERIVATIVES OF PYRAZOLINE

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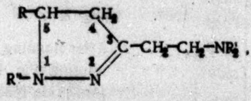
SYNTHESES

Compounds of the pyrazoline group, having the general formula (I):



(I)

in which R = phenyl, substituted phenyl, furyl-2, and NR'₂ = piperidino or dialkylamino groups, possess in a majority of cases, according to Sinha [1] a powerful local—anesthetizing action with a lower toxicity than cocaine, and cause but little irritation. Of this series, the most effective was found to be the 2'-n-butoxy compound.

On the basis of this data, the authors elected to synthesize, in the form of the hydrochloride salt, 1-phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline as a representative of these new local-anesthetizing agents.

For spectrophotometric comparison, 1,5-diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride was also prepared, using benzalacetone.

Benzalacetone was prepared according to Schmidt [2] from benzaldehyde and acetone. The resulting benzalacetone was distilled at 137-140°, 16 mm, and after standing for some time, solidified to crystals with m.p. 141°. According to Claisen and Ponder [3], the b.p. is 151-153° at 25 mm, with a m.p. of 41-42°.

1-N-Piperidino-5-phenyl-Δ^4-penten-3-one hydrochloride was synthesized according to the method of Mannich and Schutz [4] by condensing benzalacetone with paraformaldehyde and piperidine hydrochloride [5]. The substance obtained was readily soluble in water, chloroform, but did not dissolve in acetone, or ethyl acetate. M.p. 180.5°. Yield was 94.6%.

The phenylhydrazone of 1-N-piperidino-5-phenyl-Δ^4-pentene-3-one hydrochloride was obtained according to Mannich and Schutz [4] and Nisbet [6]. After recrystallization from 95% alcohol, the resulting yellow needles melted at 169°. The above-indicated phenylhydrazone was isomerized to the 1,5-diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride. The white needles were recrystallized from absolute alcohol, m.p. 197°.

1-Phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride was prepared according to Levvy and Nisbet [7], proceeding from 2-hydroxybenzalacetone, prepared according to Harris [8] from salicylic aldehyde and acetone. Recrystallization was carried out with benzene and animal charcoal. Crystals resulted with a m.p. of 139°; according to Tiemann and Kees [9], m.p. is 139°. 2-n-Butoxybenzalacetone was prepared from 2-hydroxybenzalacetone by conversion to the phenolate and reacting with n-butyl bromide, or n-butyl-p-toluenesulfonate, the latter giving the better result. 2-n-Butoxybenzalacetone had a b.p. of 171.5° at 3 mm.

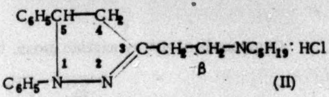
1-N-Piperidino-5-(2'-n-butoxyphenyl)-Δ^4-penten-3-one hydrochloride was synthesized according to Levvy and Nisbet [7]. The resulting white needles had a m.p. of 164.5° after recrystallization from alcohol. Yield was 28%.

15 g of the above-indicated aminoketone hydrochloride was dissolved in 120 ml of 95% alcohol, 7 g of phenylhydrazine added, and then 7.5 g of glacial acetic acid. Upon heating to 40° for a certain length of time, yellow phenylhydrazone needles separated. After recrystallization from alcohol, m.p. was 155.5°; according to Levvy and Nisbet, m.p. is 154-155°. The phenylhydrazone was isomerized with the help of glacial acetic

acid, according to Levvy and Nisbet [7], to the 1-phenyl-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride, m.p. 19°. Yield 77%.

Absorption Spectra

1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride (II) was investigated in alcoholic concentrations ranging from 10^{-1} to 10^{-5} molar (Fig. 1, Curve 1).



(II)

After standing for 24 hours, the same solution (Fig. 1, Curve 2) gave an absorption spectrum in which the first band was shifted 60 A toward the shorter wave lengths and the absorption minimum following the second band was decreased 1.6 times. 1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride was studied in dichloroethane, in a concentration range from 10^{-2} to $5 \cdot 10^{-5}$ molar (Fig.1, Curve 3). The band from λ = 2420 A and ε = 12000 was more pronounced than in alcoholic solution and increased in intensity 1.3 times.

From a comparison of the absorption spectra (Table 1) of 1,5-diphenyl-3-(β-N-piperidinoethyl)-pyrazoline in alcohol and in dichloroethane with the absorption spectrum of phenylhydrazine in alcohol (Fig. 1, Curves 1,2,3 and 5), it can be seen that the second band of the pyrazoline derivative corresponds to the second band of phenylhydrazine in position, but its maximum in dichloroethane solution is more intense. As far as the first pyrazoline derivative band is concerned, it is more intense than phenylhydrazine, by 16 times, and considerably wider. It is possible that this band is complex.

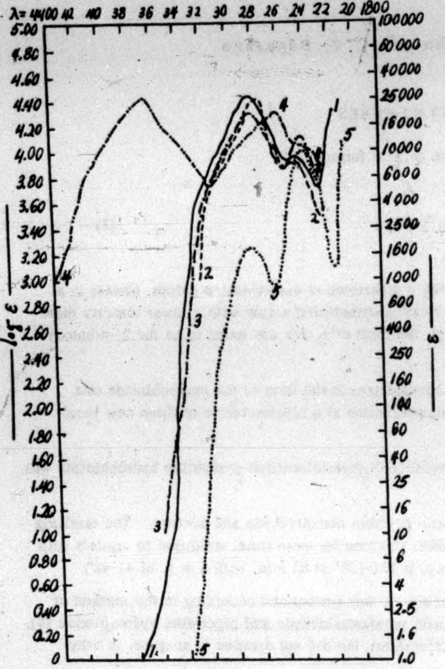
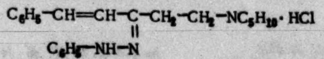


Fig. 1. 1) 1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol, from 10^{-1} - 10^{-5} molar; 2) the same from 10^{-4}-10^{-5} molar after standing 24 hours; 3) the same in dichloroethane, from 10^{-2}-$5 \cdot 10^{-5}$ molar; 4) 1-piperidino-5-phenyl-Δ^4-penten-3-phenylhydrazone hydrochloride in alcohol, from 10^{-4}-10^{-5} molar; 5) phenylhydrazine in alcohol from 10^{-1} to 10^{-4} molar.

The absorption spectrum given here (Fig. 1, Curve 4) for 1-piperidino-5-phenyl-Δ^4-penten-3-phenylhydrazone hydrochloride (III), from which was obtained the investigated pyrazoline derivative, gave indication of a wide, intense band in a 10^{-4} - 10^{-5} molar alcoholic solution, which may be related to the hydrazone structure of the unsaturated compound, and two bands corresponding to the pyrazoline derivative bands, while the first band is displaced 220 A to the short wave lengths, and almost merges with the second band, defined here by the bend in the curve.



$$C_6H_5-CH=CH-\underset{\underset{C_6H_5-NH-N}{\|}}{C}-CH_2-CH_2-NC_5H_{10}\cdot HCl$$

(III)

TABLE 1

Name	Hydrazone band		First band		Second band	
	λ	ε	λ	ε	λ	ε
1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol			2825	25000	2473	9000
The same in dichloroethane			2825	20000	2420	12000
Phenylhydrazine in alcohol			2828	1600	2410	9000
1-Piperidino-5-phenyl-Δ^4-penten-3-phenylhydrazone in alcohol	3675	25000	2605	20000	2370	13000

This comparison indicates that both bands of the pyrazoline derivative are already present in the phenylhydrazone, and consequently are not the result of pyrazoline ring closure.

1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcoholic solution, from $2.5\cdot 10^{-4}$ to $2.5\cdot 10^{-5}$ molar plus 0.01M HCl (Fig. 2, Curve 3) gave a curve parallel to the alcoholic curve (Fig. 2, Curve 1) which possessed band maxima at λ = 2813 A and ε = 2800, and at λ = 2515 A and ε = 14000. The same solution, $4\cdot 10^{-5}$ molar + 0.01 M HCl (Fig. 2, curve 2), after standing for 24 hours, also gave two bands, more definitely separated, but the first band somewhat decreased and shifted toward the longer wave lengths; the second band more intense and shifted toward the shorter wave lengths. In a 5M solution of HCl, at concentrations from 10^{-1} to $5\cdot 10^{-5}$ molar (Fig. 2, Curve 4), the above-mentioned pyrazoline gave an absorptions similar to the curve in the presence of 0.01M HCl, but shifted somewhat to the shorter wave lengths.

1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol, from 10^{-1} to 10^{-5} molar + 10M $NaOC_2H_5$ (Fig. 3, Curve 2) gave an absorption curve shifted somewhat below that of the alcoholic curve, to the longer wave lengths; the first band maximum was decreased 1.6 times. In a $5\cdot 10^{-5}$ molar solution + 10 M $NaOC_2H_5$, after 24 hours standing (Fig. 3, Curve 3), the second absorption band was decreased in intensity to ε = 5000 at λ = 2500 A and became partially overlapping with the first band. Curve 4 (Fig. 3) in 2M-sodium alcoholate was somewhat different in shape from Curve 2 (Fig. 3) in alcoholic solution + 10M $NaOC_2H_5$, both bands being displaced to the longer waves, and having a maximum at λ = 2825 A, ε = 12 500 and λ = 2500 A, ε = 7625, while the absorption minimum below the second band was increased at the same time.

It can be seen from Table 2 that the general character of the spectrum in alcohol was preserved, but the intensity of both bands was considerably changed under the effect of alcoholic HCl, increasing at first, and then with a decreased intensity of the two bands with HCl excess. This indicated, possibly, entrance of the N-atom (2) of the pyrazoline ring into reaction with HCl. The absorption spectrum in sodium alcoholate solutions belongs to the free base, 1,5-diphenyl-3-(β-N-piperidinoethyl)-pyrazoline.

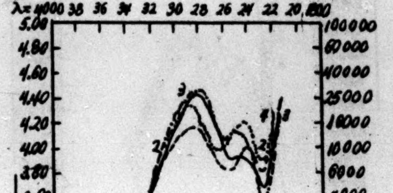


Fig. 2. 1) 1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol, from 10^{-1} to 10^{-5} molar; 2) the same, $4\cdot 10^{-5}$ molar + 0.01 molar HCl, after 24 hours standing; 3) the same, from $2.5\cdot 10^{-4}$ - $2.5\cdot 10^{-5}$ molar + 0.01M HCl; 4) the same, in 5M alcoholic HCl, from 10^{-1} to $5\cdot 10^{-5}$ molar.

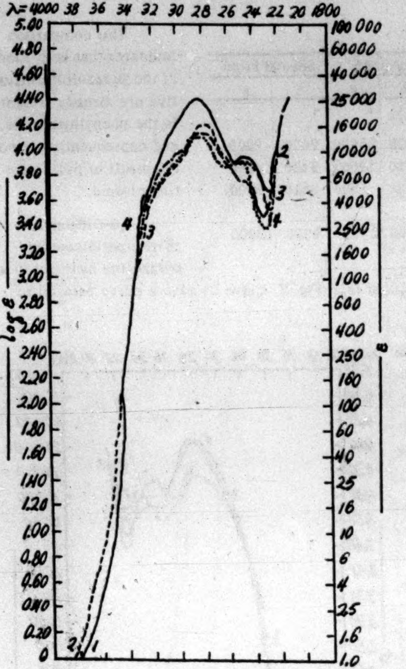


Fig. 3. 1) 1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol, from 10^{-1} to 10^{-5} molar; 2) the same, from 10^{-1} to 10^{-5} molar + 10M $NaOC_2H_5$; 3) the same, $5 \cdot 10^{-5}$ molar + 10M $NaOC_2H_5$, after 24 hours standing; 4) the same, in 2M $NaOC_2H_5$, from $4 \cdot 10^{-5}$ molar.

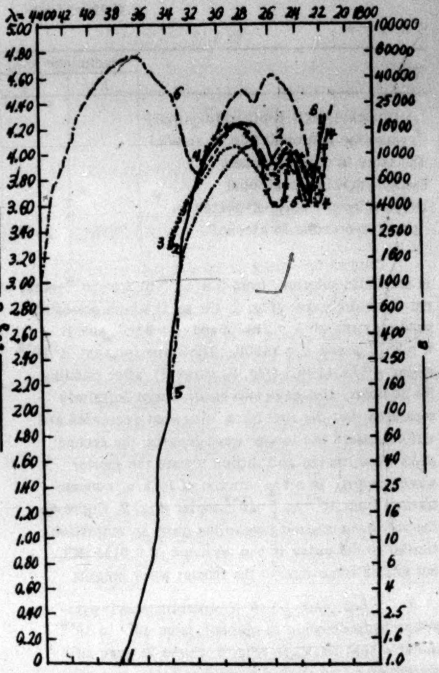
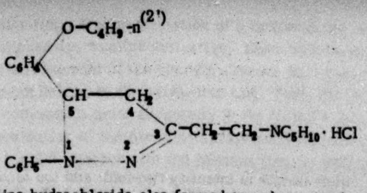


Fig. 4. 1) 1-Phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol from 10^{-4} to 10^{-5} molar; 2) the same, $5 \cdot 10^{-5}$ molar, after 24 hours standing; 3) the same, in water, $5 \cdot 10^{-5}$ molar; 4) the same, in hexane, from $4 \cdot 10^{-3}$ to 10^{-5} molar; 5) the same, in dichloroethane, from 10^{-3} to $5 \cdot 10^{-5}$; 6) 1-piperidino-5-(2'-n-butoxyphenyl)-Δ^4-penten-3-phenylhydrazone hydrochloride in alcohol, from 10^{-4} to 10^{-5} molar.

TABLE 2

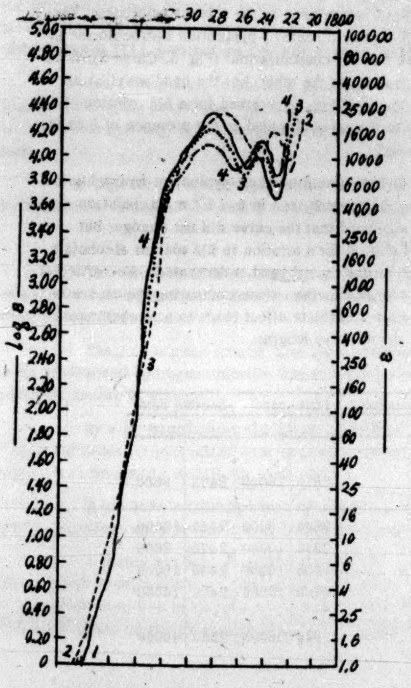
Name	First band		Second band	
	λ	ε	λ	ε
1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol	2825	25000	2473	9000
The same, + 0.01M HCl	2813	28000	2515	14000
The same, + 0.01 M HCl, after 24 hours standing	2885	20000	2425	16000
The same in 5M HCl	2850	14000	2415	10000
The same, + 10M $NaOC_2H_5$	2800	16000	2518	8000
The same, + 10M $NaOC_2H_5$, after 24 hours standing	2825	12000	2560	5500
The same, in 2M $NaOC_2H_5$	2800	12500	2560	7525

__1-Phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride (IV).__ This was studied in alcohol, in the concentration range from 10^{-1} to 10^{-5} molar. (Fig. 4, Curve 1), and the same solution in alcohol, at $5 \cdot 10^{-5}$ molar (Fig. 4, Curve 2), did not change after standing 24 hours; Curve 3 (Fig. 4) for the same pyrazoline salt in water, at $5 \cdot 10^{-5}$ molar concentration, showed a decrease in the intensity of absorption maximum by about 1.6 times, as compared with the alcoholic curve. 1-Phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-



(IV)

pyrazoline hydrochloride also formed two absorption bands when studied in hexane solution at $4 \cdot 10^{-5}$ molar concentration (Fig. 4, Curve 4), and in dichloroethane solution from 10^{-3} to $5 \cdot 10^{-5}$ molar (Fig. 4, Curve 5), but the first band in dichloroethane, as compared with the alcoholic curve, is shifted 40 A units toward the shorter wave lengths.



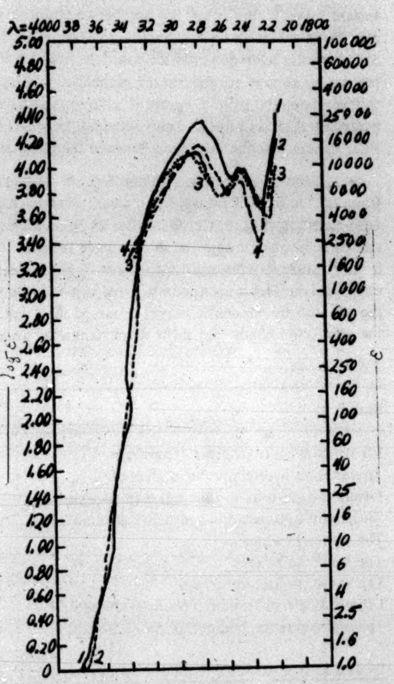
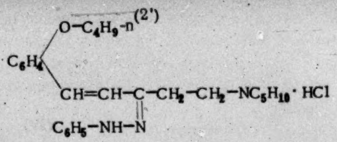


Fig. 5. 1) 1-Phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol from 10^{-4} to 10^{-5} molar; 2) the same, in 5M alcoholic HCl, from 10^{-1} to $5 \cdot 10^{-5}$ molar; 3) the same, in alcohol, from $5 \cdot 10^{-4}$ to $5 \cdot 10^{-5}$ + 0.01 M HCl; 4) the same, in 5M lcoholic HCl, from $5 \cdot 10^{-5}$M, after 24 hours standing.

Fig. 6. 1) 1-Phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)pyrazoline hydrochloride in alcohol from 10^{-1} to 10^{-5} molar; 2) the same, from 10^{-1} to $5 \cdot 10^{-5}$ molar + 10M $NaOC_2H_5$; 3) the same, $5 \cdot 10^{-5}$ M + 10M $NaOC_2H_5$ after 24 hours standing; 4) the same, in 2M $NaOC_2H_5$, from $5 \cdot 10^{-5}$ M.

1-Piperidino-5-(2'-n-butoxyphenyl)-Δ⁴-penten-3-phenylhydrazone hydrochloride (V), in alcohol from 10^{-4} to 10^{-5} molar. (Fig. 4, Curve 6) gives three absorption bands – a hydrazone band maximum at λ = 3670 Å and ε = 50000 and the following two bands at λ = 2820 Å and ε = 30000 and at λ = 2580 Å and ε = 40000. Both of these bands



(V)

correspond to the pyrazoline derivative, but the first band differs sharply in intensity, two-fold, and the second band four-fold. Thus, there occurs a very strong absorption in the range of these bands under the influence of the 2'-n-butoxy group in the phenylhydrazone of the ketone. Upon closure of the pyrazoline ring, the absorption drops and becomes even lower for the first band than for the pyrazoline derivative without the butoxy group, as comparison in Table 3 indicates.

A comparison of the butoxy derivative bands in various solvents indicated a considerable sensitivity toward solvents, but it was not possible to establish any definite relationship to the solvent polarities. The absorption spectrum for 1-phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in 5M alcoholic hydrogen chloride solution, from 10^{-1} to $5 \cdot 10^{-5}$ molar concentrations (Fig. 5, Curve 2), is expressed by a curve parallel to the alcoholic, shifting from one side to the other, but the band maxima are shifted about 100 A units toward the shorter wave lengths. Curve 4 (Fig. 5) obtained for a 5M solution of hydrogen chloride after 24 hours standing, becomes similar to the curve obtained in the presence of 0.01 M HCl, except that the minimum between the bands is decreased.

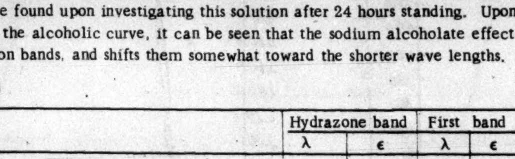
Upon investigating 1-phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride from 10^{-1} to $5 \cdot 10^{-5}$ molar, in alcohol + 10M $NaOC_2H_5$ (Fig. 6, Curve 2), and in $5 \cdot 10^{-5}$ molar solution + 10M $NaOC_2H_5$ (Fig. 6, Curve 3) after 24 hours standing, it was found that the curve did not change, but shifted somewhat toward the shorter wave lengths. Curve 4 (Fig. 6) for a solution in 2M sodium alcoholate, $5 \cdot 10^{-5}$ molar, is very similar to Curve 3, but the maximum for the second band is decreased. No particular changes were found upon investigating this solution after 24 hours standing. Upon comparing the curves in Fig. 6, with the alcoholic curve, it can be seen that the sodium alcoholate effect leads to a weakening of the absorption bands, and shifts them somewhat toward the shorter wave lengths.

TABLE 3

Name	Hydrazone band		First band		Second band	
	λ	ε	λ	ε	λ	ε
1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol			2825	25000	2473	9000
1-Phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol			2805	16000	2440	10000
The same, in water			2835	10000	2475	8000
The same, in hexane			2865	16000	2405	10000
The same, in dichloroethane			2765	10000	2468	10000
1-Piperidine-5-(2'-n-butoxyphenyl)-Δ^4-penten-3-phenylhydrazone hydrochloride in alcohol	3670	50000	2820	30000	2580	40000

Evaluation of the Spectrophotometric Data

Spectrophotometric investigations of the local anesthetic, 1-phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride (VI):



Cl, (VI)

make it possible to offer the following concept. Salt formation should proceed at the nitrogen of the more basic piperidine ring. Due to saturation of a portion of the molecule, its absorption spectrum is not reflected in that of the diphenylpyrazoline derivative. Since both bands of the diphenylpyrazoline derivative are present in the absorption spectrum of the phenylhydrazone from which the pyrazoline derivative is obtained, these bands therefore do not belong to the pyrazoline ring. From the fact that the second band in the 1,5-diphenylpyrazoline derivative corresponds quite accurately to the second band of phenylhydrazine, a deduction can be made concerning the contribution of the phenylhydrazine portion to the diphenylpyrazoline derivative spectrum, where nitrogen atoms 1 and 2 interact with the benzene ring, as with phenylhydrazine.

The first band of 1,5-diphenylpyrazoline derivatives differs by a considerably greater intensity from that of the first band of phenylhydrazine. From this fact its participation in formation of the second phenyl group also follows, with substitution in the 5th position of the pyrazoline ring. Its interaction with the pyrazoline ring and the N atom can occur only through the group $-\underset{|}{\mathrm{C}}\mathrm{H}-$. This case requires an additional spectrophotometric investigation. According to Levvy and Nisbet's investigation [10], of unsaturated piperidinoketones, from which the pyrazolines were prepared, it was found that they possess a local anesthetizing action, but are highly irritating [10]. The phenylhydrazine derivatives also possess local anesthetizing action; for example, antipyrine and tolupyrine [11], p-carbethoxyphenylhydrazine $C_2H_5OCOC_6H_4NHNH_2$ are good anesthetics [12].

In view of this fact, two atomic groupings in the molecule of the pyrazoline derivative should possess local-anesthetizing properties: the first corresponding to the unsaturated piperidinoketone hydrochloride salt with 2'-n-butoxyphenyl-(5) in the piperidine ring, and the second, corresponding to the phenylhydrazine structure.

The high local-anesthetizing action of 1-phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride is dependent upon a combination of these two local-anesthetizing groups.

SUMMARY

1. The synthesis of a new, highly-active local anesthetic, 1-phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride, and also of 1,5-diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride, has been worked out.

2. Their absorption spectra have been investigated in alcohol, hexane, dichloroethane, water, in alcoholic solutions of hydrogen chloride, and of sodium alcoholate, and, in addition, the absorption spectrum for phenylhydrazine in alcohol.

3. By a spectrophotometric investigation, three strong absorption bands for the phenylhydrazones, and two strong bands for pyrazoline have been determined; thus absorption spectra can serve for their differentiation, which frequently is difficult to do chemically.

4. It has been established that the absorption bands for the investigated pyrazoline derivatives are not solely dependent upon interaction of the phenyl radicals with the nitrogen atoms of the pyrazoline ring.

5. A theory has been suggested that the high local-anesthetizing action of 1-phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride is conditioned by a combination of two groupings of atoms between 2'-n-butoxyphenyl-(5) and the piperidine ring, and a part of which corresponds to the phenylhydrazine group on the pyrazoline ring.

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CHEMICAL STRUCTURE AND PARASITICIDAL ACTIVITY

XII. DICHLOROISOMERIC MESO-ALKYLAMINOALKYLAMINOACRIDINES AND THEIR ANTIMALARIAL PROPERTIES

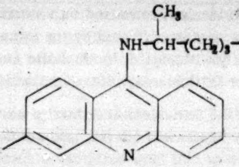
A. F. Bekhli

In the preceding work from the author's laboratory [1] there was described the synthesis for a series of physiologically-active, alkoxy-free compounds of the acridine series, which showed, upon comparison with their alkoxyl analogs, activity.

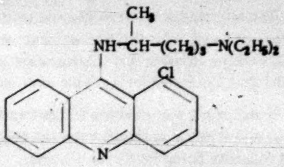
This deduction was made on the basis of a comparison of the properties of compounds of this type; as the essence of the present work, however, is the significant fact that 6-chloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine (methoxyl-free atebrin) (I) is almost equal to atebrin in its antimalarial activity.

On the other hand, among the group of chloroisomeric 9-(4'-diethylamino-1'-methylbutyl)-aminoacridines [2] synthesized by the author, 1-chloro 9-(4'-diethylamino-1'-methylbutyl)-aminoacridine (II) exceeded by approximately 40% the antimalarial action of atebrin.

In 1946 an article by Spaulding and co-workers [3] appeared, concerning the synthesis of 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine (III), which possessed an antimalarial action, by test with P. gallinaceum, which exceeded that of atebrin.

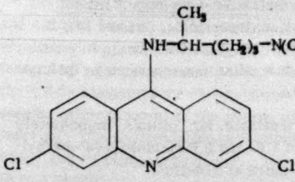


(I)



(II)

From a comparison of this work with the data given above, it seemed expedient to the author to synthesize that group of dichloroisomers of 9-dialkylaminoalkylaminoacridines wherein one chlorine is in the 6-position, i.e., in one benzene portion of the acridine nucleus, and the second is introduced in various positions of the second benzene portion of the acridine nucleus. From a knowledge of the activity of methoxyl-free atebrin (I) which contains chlorine in the 6-position, it is possible to determine how the introduction of a second halogen will affect the antimalarial activity of the corresponding acridine derivative. Therefore, the following compounds were selected for synthesis:



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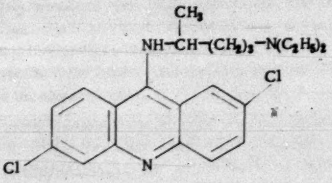

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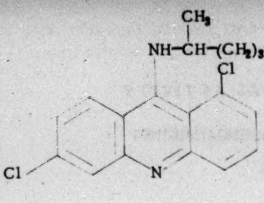
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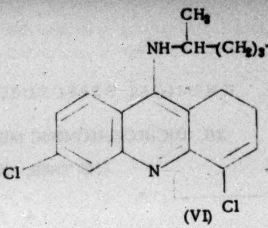
(VI)

It should be mentioned that Spaulding and co-authors, during synthesis of 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine, obtained an intermediate 3,6,9-trichloroacridine by condensing 4-chloro-2-nitrobenzaldehyde with chlorobenzene, with subsequent treatment of the resulting 3,6-dichloroacridone by phosphorous oxychloride. The American authors preferred this procedure to the Uhllmann reaction from 2,4-dichlorobenzoic acid and m-chloroaniline, because of the low yield of 3,5'-dichlorodiphenylamino-2'-carboxylic acid (5.8%) which was simultaneously obtained.

The authors pointed out another limitation of the Uhllmann condensation, namely, that they foresaw the task of separating the isomeric trichloroacridines which would result upon treatment of 3,5'-dichlorodiphenylamine-2'-carboxylic acid with phosphorous oxychloride — ring closure occurring in the o- and p-positions with regards to the substituent present in the ring.

Nevertheless, the author decided to synthesize the selected compounds (III IV) by the method which was abandoned by the American authors mentioned. By carrying out the Uhllmann reaction in an aqueous medium under conditions developed by the author, it was possible to increase to 53% (Spaulding gave 5.8%) the yield of 3,5'-dichlorodiphenylamino-2'-carboxylic acid.

The resulting acid, upon heating with phosphorous oxychloride, was converted into a mixture of the isomeric 1,6,9- and 3,6,9-trichloroacridines. Separation of the isomers was effected by the established fact that the resulting isomeric trichloroacridines vary in their solubility with regard to alcoholic ammonia. It was found that 1,6,9-trichloroacridine goes into solution, while 3,6,9-trichloroacridine remains insoluble.

It was noted that chlorine in position 9 of both 1,6,9- and 3,6,9-trichloro-acridines possesses a high mobility, and that the products, upon standing even for brief time in air, will convert into acridone, the greatest mobility being for the first isomer.

It was found that if the mixture of isomeric trichloroacridines was not separated, and then, after standing for a short time in air, condensed with a side chain, that a considerable quantity of acridone was then isolated; it was possible to isolate, then, as the condensation product, pure 3,6-dichloro-9(4'-diethylamino-1'-methylbutyl)-aminoacridine. If the dichloroacridone separated during the reaction is converted by phosphorous oxychloride into the trichloroacridine, there then results a product which, according to its melting point, corresponds to 1,6,9-trichloroacridine. This example illustrates clearly that the meso-halogen in 1,6,9-trichloroacridine has a greater mobility than in 3,6,9-trichloroacridine.

The separated isomeric trichloroacridines were condensed with 1-diethylamino-4-aminopentane in phenol, and there were separated dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridines (III and IV), in the form of the dihydrochlorides, with melting points, respectively, of 230-231° and 183-184°. From dihydrochloride (III) the base, 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine was separated in the crystalline form, m.p. 81°.

If the freshly-prepared isomeric mixture of trichloroacridines is not separated, but, instead, immediately condensed with 1-diethylamino-4-aminopentane, then an isomeric mixture of 1,6- and 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridines results, the dihydrochloride of which melts at 210-212°.

2,6- and 4,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridines (V and VI) were obtained in the usual manner by condensing the corresponding 2,6,9- and 4,6,9-trichloroacridines with 1-diethylamino-4-aminopentane in phenol.

The indicated trichloroacridines were prepared by ring closure of 4,5'- and of 2,5'-dichlorodiphenylamino-2'-carboxylic acids with phosphorous oxychloride. The isomeric dichlorodiphenylaminocarboxylic acids were obtained by condensing 2,4-dichlorobenzoic acid with o- and p-chloroanilines. The dihydrochloride of 2,6-dichloro-9-(4'-

diethylamino-1'-methylbutylene)-aminoacridine, and the corresponding intermediate products, have been described by O. Yu. Magidson, A.M. Grigorovsky and E. Galperin [4]. The author has isolated for the first time the base, 2,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine.

The described compounds, in the form of their hydrochloride salts, were tested for their antimalarial action on an avian malaria. The effectiveness was determined with regards to the erythrocytic stages of the parasite during Plasmodium relictum blood infection. It was found at the time that the isomeric mixture of 1,6- and 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine possessed the greatest activity, the 3,6-dichloroisomer a greater activity than that of atebrin, the 2,6-dichloroisomer active, but less so than atebrin, and finally the 4,6-dichloroisomer, which was found to be completely inactive. With in vivo toxicity studies on mice, the 3,6- and 1,6-dichloroisomers, as well as the isomeric mixture, were found to be less toxic than atebrin; the 2,6-dichloroisomer was found to be more toxic than atebrin.

These tests were carried out in the protozoological division of the institute by Prof. Sh. D. Moshkovsky and the senior, scientific worker, S.A. Syrkina, to whom the author expresses his appreciation.

EXPERIMENTAL

3,5-Dichlorodiphenylamino-2'-carboxylic Acid. 78 g of 2,4-dichlorobenzoic acid, 100 g of m-chloroaniline, 90 g of potash, 70 ml of water and 1 g of copper acetate were heated at the boiling point for 21 hours (temperature in the flask was 110-120°).

After removal of unreacted m-chloroaniline (62 g) by steam distillation, the residue was heated with animal charcoal, filtered and acidified with hydrochloric acid to a neutral reaction. 61.2 g, or 53% of theory yield, of 3,5'-dichlorodiphenylamino-2'-carboxylic acid was isolated; after recrystallization from aqueous alcohol, the acid melted at 196° (Spaulding indicated 196-198°). Upon acidification of the filtrate to an acid reaction, 26.5 g of 2,4-dichlorobenzoic acid, which did not enter into reaction, was isolated.

The Mixture of 1,6,9- and 3,6,9-Trichloroacridines and Its Separation. 30 g of 3,5-dichlorodiphenylamino-2'-carboxylic acid, 50 ml of chloroform and 20 ml of phosphorous oxychloride were heated for 4 hours on a water bath. After distilling off the chloroform, the residue was poured onto ice, treated with ammonia, filtered with suction and washed with water. 30 g of crude product was isolated (or 99% of theoretical yield), which represented a mixture of 1,6,9- and 3,6,9-trichloroacridines.

The resulting mixture of isomers was heated in water-alcoholic ammonia (300 ml of alcohol + 30 ml of 25% ammonia) to boiling and the hot solution filtered off; the 3,6,9-trichloroacridine remained on the filter and the 1,6,9-trichloroacridine went into solution.

16.4 g of 3,6,9-trichloroacridine resulted, which, after crystallization from heptane, and upon immersion of the capillary into preheated sulfuric acid, melted at 220° (Spaulding gives 225°).

After addition of water to the alcoholic-ammoniacal filtrate, 1,6,9-trichloroacridine precipitated (5.6 g), which, after crystallization from heptane, melted at 144-146°.

8.280 mg substance: 0.382 ml N_2 (21°, 756 mm). 9.071 mg substance: 0.412 ml N_2 (21°, 756 mm). Found %: N 5.32, 5.24. $C_{13}H_6NCl_3$. Calculated %: N 4.95.

1,6-Dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine. To a melt, consisting of 15 g of phenol and 4.0 g of 1-diethylamino-4-aminopentane, was added with vigorous stirring, finely-ground 1,6,9-trichloroacridine (6.3 g), while heating on a boiling water bath. The mixture was heated for 1 hour, and was then poured into a 10% solution of caustic soda. The separated oil was washed twice with water and dissolved in benzene, and the 1,6-dichloroacridone (0.7 g) formed during the reaction was filtered off. The benzene solution was dried with potash. After removal of the potash, alcoholic hydrochloric acid was added to the benzene solution to a Congo reaction. The hydrochloride separated as an oil, which, after solution in absolute alcohol with the addition of ether, and standing, crystallized. The product was filtered by suction, washed with acetone. The yield was 3 g, m.p. 179-180°.

1,6-Dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine hydrochloride crystallized out from alcoholic-ether mixture in the form of fine, yellow prisms, with m.p. 183-184°.

The product was soluble in water and alcohol, but did not dissolve in ether or acetone.

0.1999 g substance: 0.0081 g H_2O. 0.2566 g substance: 0.0095 g H_2O. Found %: H_2O 4.05, 3.70. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl \cdot H_2O$. Calculated %: H_2O 3.63 0.2415 g substance: 0.1420 g AgCl. 6.125 mg substance: 0.499 ml N_2 (27°, 746 mm). 5.588 mg substance: 0.460 ml N_2 (27°, 746 mm). Found %: Cl(ionic) 14.54; N 9.09, 9.19. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl$. Calculated %: Cl (ionic) 14.86; N 8.80.

3,6-Dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine. This compound resulted from 3,6,9-trichloroacridine (7.5 g) and 1-diethylamino-4-aminopentane (4.5 g) in phenol (15 g), by a procedure identical with that described above. There was separated from the reaction mass 1.6 g of 3,6-dichloroacridone: 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine dihydrochloride resulted in the form of a yellow powder, m.p. 230-231° (Spaulding gives 235°) in the amount of 3.2 g. A mixed sample with the 1,6-dichloroisomer gave a depression, melting at 169-175°.

The product was soluble in water and alcohol but did not dissolve in acetone or ether.

Found %: H_2O 3.89. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl \cdot H_2O$. Calculated %: H_2O 3.63. Found %: Cl (ionic) 14.58; N 9.11, 8.99. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl$. Calculated %: Cl (ionic) 14.86; N 8.80.

The base, 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine, was obtained by the addition of an ammonia solution to an aqueous solution of the hydrochloride; the resulting oil crystallized from aqueous acetone, m p. 81°.

0.0772 g substance: 0.0029 g H_2O. 0.1623 g substance: 0.0072 g H_2O. 4.742 mg substance: 0.412 ml N_2 (22°, 744 mm). 4.441 mg substance: 0.392 ml N_2 (22°, 744 mm). Found %: H_2O 3.75, 4.43; N 9.84, 9.99. $C_{22}H_{27}N_3Cl_2 \cdot H_2O$. Calculated %: H_2O 4.26; N 9.95.

Condensation of a Mixture of 1,6,9- and 3,6,9-trichloroacridine with 1-Diethylamino-4-aminopentane. After standing for some time (the product partially hydrolyzing the acridone), the unseparated mixture of isomeric trichloroacridines (6 g) was condensed with 1-diethylamino-4-aminopentane (4.5 g) in phenol (15 g) by the procedure described above. 3 g of acridone was separated from the reaction mass.

1.5 g of the condensation product, in the form of the hydrochloride, with m.p. 230°, resulted, a mixed sample with 3,9-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine of which did not give a depression in melting point. From the hydrochloride solution a base was separated by 25% ammonia solution, which crystallized from aqueous acetone; m.p. 81-82°. A sample, mixed with the base, 3,9-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine, did not give depression.

Hence, it may be considered that in the case given a pure product, 3,6,-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine was obtained; 1,6,9-trichloroacridine, a more unstable product, was hydrolyzed to acridone. For verification of this assumption, the dichloroacridine separated from the reaction was converted, by the aid of phosphorous oxychloride, into trichloroacridine, which had an m.p. of 142°, and was found to be identical with 1,6,9-trichloroacridine.

Condensation of a Freshly-Prepared Isomeric Mixture of 1,6,9- and 3,6,9-Trichloroacridines with 1-Diethylamino-4-aminopentane (III and IV). The isomeric mixture (51.2 g) of 1,6,9- and 3,6,9-trichloroacridines (recrystallized from benzene, m.p. 190°) was added to the melt consisting of 103 g of phenol and 28 g of 1-diethylamino-4-aminopentane, with vigorous stirring and with heating on a water bath. The mixture was heated, with stirring, for an additional hour, and the mass then poured into 10% caustic soda solution. The viscous oil which separated was washed several times with water, the water poured off, and the oil dissolved in acetone. The acridone formed during the reaction did not dissolve in acetone and was filtered off.

Alcoholic hydrogen chloride was added to the acetone solution, and the hydrochloride which formed separated out first as an oil, which, after some standing, and stirring with a glass rod, crystallized. The product was filtered off with suction and was washed with dry acetone. The yield of crude product varied from 62 to 82% of the theoretical. The dihydrochloride of the isomeric mixture of 1,6- and 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridines was crystallized from aqueous acetone, dissolved in the minimal volume of water with heating, and to the solution was then added animal charcoal, the mixture filtered, and acetone added to the cooled filtrate. A fine, yellow, crystalline powder resulted, m.p. 210-212°.

2,5'-Dichlorodiphenylamino-2'-carboxylic acid. 160 g of 2,4-dichlorobenzoic acid, 200 g of o-chloroaniline, 185 g of potash, 145 ml of water and 2.26 g of copper acetate were heated on an oil bath at 140-150°

for 28 hours. After removal of the unreacted o-chloroaniline (146 g) by steam distillation, the residue was heated with animal charcoal, filtered, and acidified with hydrochloric to the neutral point. 51 g, or 21.6% of theoretical yield of 2,5-dichlorodiphenylamino-2'-carboxylic acid was isolated.

After purification by reprecipitation and by crystallization from aqueous alcohol, the acid melted at 228-229°.

6.625 mg substance: 0.304 ml N_2 (25°, 748 mm). 6.530 mg substance: 0.333 ml N_2 (24°, 748 mm). Found %: N 5.17, 5.76. $C_{13}H_9O_2NCl_2$. Calculated %: N 4.96.

4,6,9-Trichloroacridine. 43.3 g of 2,5-dichlorodiphenylamino-2'-carboxylic acid, 95 ml of dichloroethane and 40 ml of phosphorous oxychloride were heated for 4 hours on a water bath. After distilling off the chloroform, the residue was poured onto alkalized ice, filtered by suction and washed with water. The product crystallized from benzene. Cream-colored prisms, m.p. 177-178°, weight 24 g. Soluble in benzene, alcohol; insoluble in water.

7.623 mg substance; 0.372 ml N_2 (28°, 739 mm). 7.520 mg substance: 0.353 ml N_2 (22°, 742 mm). Found %: N 5.38, 5.30. $C_{13}H_6NCl_3$. Calculated %: N 4.95.

4,6-Dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine. 11.5 g of 4,6,9-trichloroacridine was condensed with 6.3 g of 1-diethylamino-4-aminopentane in phenol (25 g) with heating on a water bath. The condensation product was poured into a solution of 10% alkali, the separated oil washed several times with water, and then dissolved in acetone. To the dried acetone solution of base, alcoholic hydrogen chloride was added to an acid Congo reaction. The oil which separated on standing solidified. The product was recrystallized from a mixture of alcohol and acetone. Fine yellow crystalline powder, m.p. 194°. Yield of pure product was 7.3 g.

The dihydrochloride was readily soluble in water and alcohol, insoluble in acetone and ether.

0.2009 g substance: 0.0080 g H_2O. 0.2022 g substance: 0.1159 g AgCl. Found %: H_2O 3.98; Cl (ionic) 14.18. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl \cdot H_2O$. Calculated %: H_2O 3.68; Cl (ionic) 14.32. 8.640 mg substance. 0.666 ml N_2 (26°, 748 mm). 6.599 mg substance: 0.540 ml N_2 (26°, 748 mm). Found %: N 8.66, 9.19. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl$. Calculated %: N 8.80.

The base, 4,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine was obtained by treatment of an aqueous solution of the dihydrochloride with ammonia, the separated oil crystallizing after standing, and after recrystallization from aqueous acetone, yellow plates, m.p. 67-68° resulted. The compound was soluble in a majority of the organic solvents, and contained water of crystallization which was removed either by heating with phosphorous pentoxide at 50°, or by prolonged standing in a desiccator, whereupon the crystalline product converted to an oil.

9.141 mg substance: 0.784 ml N_2 (23°, 741 mm). 7.784 mg substance: 0.686 ml N_2 (25°, 743 mm). 0.1588 g substance: 0.0071 g H_2O. Found %: N 9.64, 9.86; H_2O 4.47. $C_{22}H_{27}N_3Cl_2 \cdot H_2O$. Calculated %: N 9.95; H_2O 4.26.

4,5-Dichlorodiphenylamino-2'-carboxylic acid and 2,6,9-trichloroacridine were obtained by the method described by O. Yu. Magidson and coworkers [4].

2,6-Dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine. 15.3 g of 3,6,9-trichloroacridine was condensed with 5.5 g of 1-diethylamino-4-aminopentane in phenol medium (30 g) by the method described above.

4.4 g of 2,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine dihydrochloride separated. The product crystallized from aqueous acetone in the form of tetrahedral plates, which softened at 190° and melted at 226°.

0.2370 g substance: 0.0110 g H_2O. 0.2012 g substance: 0.0096 g H_2O. 7.445 mg substance: 0.539 ml N_2 (26°, 749 mm). 7.325 mg substance: 0.549 ml N_2 (26°, 747 mm). Found %: H_2O 4.64, 4.77; N 8.14, 8.40. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl \cdot 1.25\ H_2O$. Calculated %: H_2O 4.50 N 8.40. 0.2260 g substance: 0.1352 g AgCl. 0.1859 g substance: 0.1101 g AgCl. 5.682 mg substance: 0.451 ml N_2 (22°, 757 mm). Found %: Cl (ionic) 14.80, 14.65; N 9.14. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl$. Calculated %: Cl (ionic) 14.86; N 8.80.

The base, 2,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine was obtained by treatment of an aqueous solution of the hydrochloride with alkali. The product crystallized from aqueous acetone in yellow plates, m.p. 78-79°.

It dissolved in a majority of the organic solvents, but was insoluble in water.

0.1264 g substance: 0.0068 g H_2O. 6.177 mg substance: 0.549 ml N_2 (21°, 756 mm). 6.145 mg substance: 0.530 ml N_2 (21°, 756 mm). Found %: H_2O 5.38; N 10.26, 9.96. $C_{22}H_{27}N_3Cl_2 \cdot 1.25 \cdot H_2O$. Calculated %: H_2O 5.27; N 9.84.

SUMMARY

1. 2,5'-, 3,5'- and 4,5'-dichlorodiphenylamino-2'-carboxylic acids have been obtained by condensing 2,4-dichlorobenzoic acid with o-, m- and p-chloroanilines. 3,5'-Dichlorodiphenylamino-2'-carboxylic acid was obtained in 53% yield of theory.

2. By the interaction of 3,5'-dichlorodiphenylamino-2'-carboxylic acid with phosphorous oxychloride, there has been obtained a mixture of the isomeric 1,6,9- and 3,6,9-trichloroacridines, which have been separated on the basis of their differential solubility in aqueous-alcoholic ammonia; the remaining isomeric trichloroacridines, 2,6,9- and 4,6,9-, have been obtained by heating 4,5'- and 2,5'-dichlorodiphenylamino-2'-carboxylic acids with phosphorous oxychloride.

3. 1,6-, 2,6-, 3,6- and 4,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridines, and mixture of isomers 1,6- and 3,6- dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridines, have been synthesized by condensation of the corresponding trichloroacridines with 1-diethylamino-4-aminopentane.

4. The resulting dichloroisomers of 9-(4'-diethylamino-1'-methylbutyl)-aminoacridine, in the form of their hydrochloride salts, have been biologically tested with Plasmodium relictum.

According to the data of Prof. Sh. D. Moshkovsky and senior scientific -worker, S.A. Syrkina, the preparations have shown the following activities. The isomeric mixture of 1,6- and 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridines and the 3,6-dichloroisomer, possess the highest activities, exceeding that of atebrin; the 1,6-dichloroisomer is approximately equal to that of atebrin, the activity of the 2,6- dichloroisomer is less than the activity of atebrin, and the 4,6-dichloroisomer possesses no antimalarial activity.

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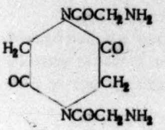
THE MICROSTRUCTURE OF PROTEIN

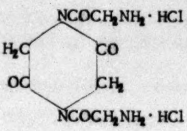
XII. SYNTHESIS OF THE FREE N-AMINOACYL COMPOUND OF DIKETOPIPERAZINE AND OF ITS DERIVATIVES

L. N. Akimova and N. I. Gravrilov

In the preceding article [1] the authors demonstrated that it was possible to synthesize the N-acylamino derivative of diketopiperazine by protecting the amino group of the amino acid through the acyl derivatives. Abderhalden [2] was the first to express his thought on the matter of a possible linkage of diketopiperazine with amino acids through nitrogen of the first. During the last 25 years of his life, he tried unsuccessfully to carry out this reaction. Apparently, his failures in this work forced him to renounce the diketopiperazine theory [3]. In the present work the authors describe the synthesis of free N,N'-diglycyldiketopiperazine (I), its HCl salt (II), its carbobenzoxyderivative (III), and the carbobenzoxy derivative of N,N'-diglycylalanine (IV):



(I)



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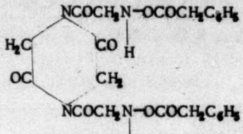
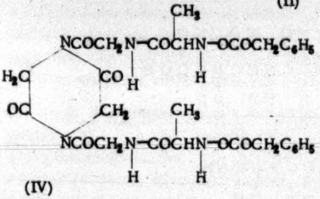


(III)

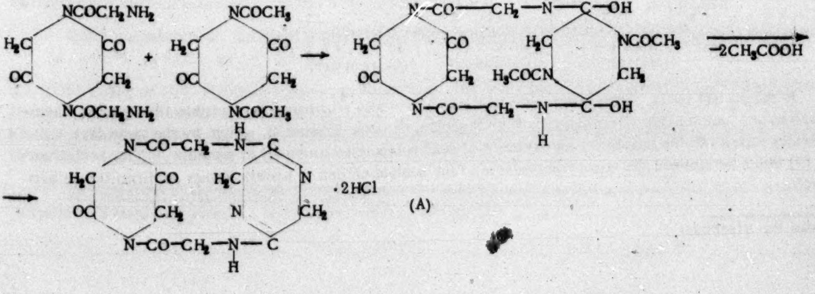


(IV)

These experiments make it possible to consider that N,N'-amino acid derivatives of diketopiperazine are easy to synthesize, and by the modern Bergmann method [4] can be elongated to form a peptide chain, but they give a biuret reaction only because of asymmetric cleavage of the ring. The authors doubt that these derivatives play an important role in the structure of the protein protoacid (S. S. Perov [5]), but it is possible that this linkage acts as a prosthetic group of the protein (S. S. Perov anticomplex). The authors have studied further both the synthesis of these linkages and the properties of model structures. It is not excluded that the complexity of the molecule approximates the properties of a peptone structure (molecular structure, Fodor acropeptide).

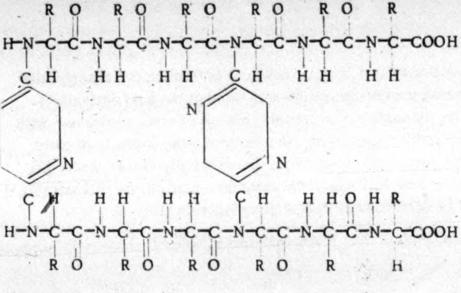
In our model, the synthesis of which we are carrying out at the present time, 2 diketopiperazines are linked with two tripeptides. At the moment, in N,N'-diglycyldiketopiperazine, the authors have realized a construction model of such structure, very easy to synthesize (Scheme 1, A):

Scheme 1

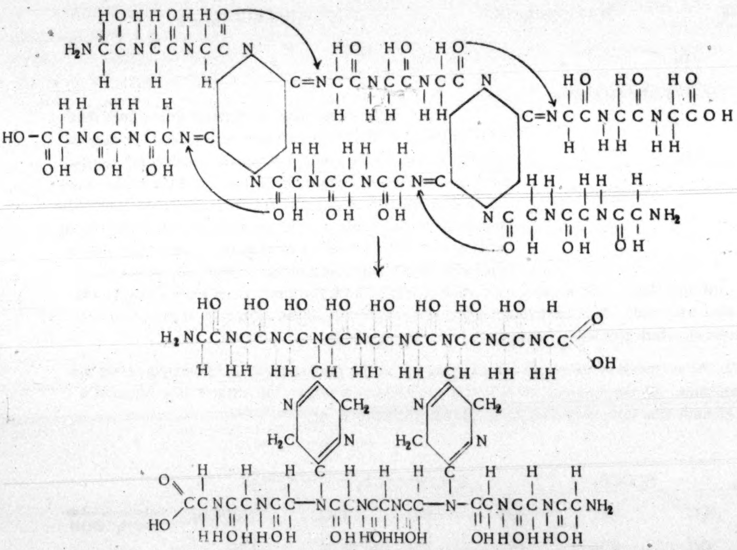


This compound shows that derivatives of N,N'-substituted diketopiperazine have free rotation and may form bridges between the diketopiperazines. This property makes certain the fact that the authors' molecular structure (2 hexapeptides linked to 2 dihydropiperazines) (vide Scheme 2), and the molecular structure on the basis of Levine's hypothesis [6], discussed elsewhere by the authors and based upon N,N'-acylaminodiketopiperazine conversions, will be shortly carried out (vide Scheme 3).

Scheme 2



Scheme 3



In the present series, the authors' works have experimentally established two possible linkages for diketopiperazines and amino acids: 1) amidine, and 2) N-acylamine (Vide Scheme 4), which, by the same fact completely eliminates the possibility for existence of dead polypeptide structures of protein*. M. I. Plekhan's works [7] which determined the tripeptide structure of the peptide portion of protein further confirms the authors' assertions.

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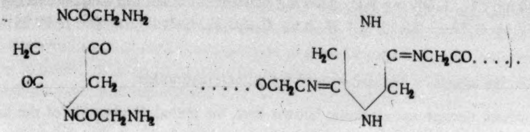
* Beyond the tripeptides.

Scheme 4



EXPERIMENTAL

1. Acylation of diketopiperazine by N-carboglycinealdehyde. 1.1 g of N-carboglycineanhydride, synthesized according to Leuchs [8], was ground in a mortar with 0.62 g of diketopiperazine. 20 ml of dry xylene was added and heated in Wood's metal to the cessation of CO_2 evolution (absorbant – a solution of baryta water). The precipitate was filtered and washed on the filter with cold water. A portion of the precipitate dissolved. The undissolved portion, with negative anhydride and ninhydrin reactions, gave a biuret reaction of the tripeptide type (upon standing with alkali). The aqueous filtrate from the precipitate was evaporated to dryness in vacuo with heat. By reactions (dipeptide biuret and anhydride), the resulting substance was found to be diketopiperazine. The precipitate, giving a tripeptide biuret reaction, represented a glycine polymer of unknown structure.

Upon repeating this experiment, preliminary heating of diketopiperazine with N-carboglycineanhydride was carried out on a water bath (boiling); here, no evolution of CO_2 occurred. However, an increase in temperature (heating in Woods metal at 142°) caused reaction, and strong CO_2 evolution occurred. From this experiment, as well as from the above-described, diketopiperazine and glycine polymer were isolated.

Thus the attempt directly to aminoacylate diketopiperazine, for the purpose of obtaining free N,N'-aminoacyldiketopiperazine, failed. The desire to synthesize free N,N'-diglycyldiketopiperazine led the authors to consider a different procedure. Having abandoned the attempt to synthesize this compound directly, the authors utilized its earlier-synthesized derivatives. Among the literature methods for removal of acyl groups in amino acid derivatives (peptides), the most appropriate was found to be elimination of the phthalyl substituent with the aid of hydrazine hydrate, which the authors therefore used.

2. The interaction of 1,4-diphthalylglycyl-2,5-diketopiperazine with hydrazine hydrate. In absolute alcohol medium. a) 0.25 g (0.02 mole) of hydrazine hydrate and 30 ml of absolute ether was added to 1.22 g of N,N'-diphthalylglycyldiketopiperazine. The solution was shaken for 1 hour on a rocker. The resulting precipitate was filtered off and washed on the filter with alcohol. The precipitate and the filtrate were analyzed separately. Upon standing, a precipitate separated from the alcoholic filtrate which was filtered off and washed with ether. The substance was recrystallized from boiling 50% alcohol. The resulting precipitate did not give the anhydride and ninhydrin reactions, did not melt above 340°, and was found to be the phthalylhydrazide.

2.405 mg substance: 0.372 ml N_2 (25°, 730 mm). 2.285 mg substance: 0.365 ml N_2 (25°, 730 mm).
Found %: N 17.1; 17.2. $C_8H_6O_2N_2$. Calculated %: N 17.28.

Precipitate. This was treated with aqueous alcohol. Upon standing at room temperature, crystals separated out from the filtrate, which were filtered off and washed with alcohol and ether. Dried in vacuo over P_2O_5. The melting point by rapid heating (on a thermometer) was 245°; upon slow heating in a sealed capillary, the substance decomposed at 220°. Insoluble in water, gave the anhydride (by the usual procedure) and the ninhydrin reactions with 5-minute heating reactions. Crystalline form under the microscope – well-formed rectangles.

3.055 mg substance: 2.208 ml 0.2 N solution $KH(IO_3)_2$. 3.930 ml substance: 2.824 ml 0.2 N solution $KH(IO_3)_2$.
Found %: N 20.25, 20.12. $C_{24}H_{24}O_8N_8$.

b) 1.22 g of N,N'-diphthalylglycyldiketopiperazine was mixed with 0.5 g (0.04 mole) of hydrazine hydrate in 30 ml of absolute alcohol. The solution was shaken on a rocker for 5 hours. After completion of the reaction, the alcoholic filtrate, basic to litmus, was separated from the filtrate and washed with alcohol (to a neutral reaction in the alcoholic filtrate).

Investigation of the alcoholic filtrate. During the concentration, a substance separated which was recrystallized from 50% alcohol. Its complete analysis was carried out.

3.602 mg substance: 0.552 ml N_2 (23°, 744 mm). 7.005 mg substance: 1.067 ml N_2 (21°, 748 mm). 3.165 mg substance: 6.879 mg CO_2; 1.065 mg H_2O. ~~3100~~ mg substance: 6.733 mg CO_2; 0.970 mg H_2O. Found %: N 17.30, 17.40; C 59.31, 59.27; H 3.76, 3.50. $C_8H_6O_2N_2$. Calculated %: N 17.28; C 59.26; H 3.70.

From analysis and properties, the substance isolated represented phthalylhydrazide.

Dry hydrogen chloride was passed through the alcoholic filtrate from the phthalylhydrazide of the basic reaction. The resulting precipitate was filtered off and washed with alcohol. M.p. 198°. By the properties (insoluble in alcohol, readily soluble in water, reducing copper during the biuret reaction, positive ninhydrin reaction) and by the melting point, the substance was found to be the hydrazine hydrochloride.

Determination of amino nitrogen according to Sorenson-Gavrilov. 0.0960 g of the substance: 9.3 ml of 0.2 N NaOH (respectively, 17.88 ml of 0.1 N H_2SO_4) Found %: N 26.67. $H_6N_2Cl_2$. Calculated %: N 26.66.

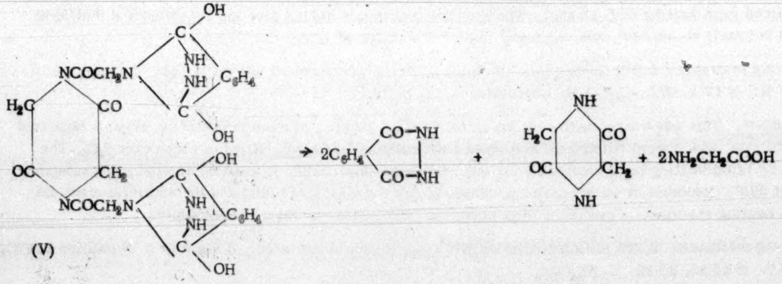
Titration according to Willstätter. 0.0894 g of the substance: 16.25 ml of 0.1 N alcoholic NaOH (respectively, 16.97 ml of 0.1 N H_2SO_4). Found %: N 26.58. $H_6N_2Cl_2$. Calculated %: N 26.66.

Treatment of the precipitate. The precipitate was treated on a filter at room temperature with 50% alcohol. Here a small portion of the precipitate was undissolved (in it were crystals of the initial substance). From the water-alcohol filtrate, upon standing for 24 hours, a substance separated which was filtered off and washed repeatedly with water (because of possible presence of diketopiperazine) and then with alcohol. Under the microscope, this substance represented very active crystals in polarized light, in the form of rectangular plates. M.p. about 220°, with decomposition. The anhydride reaction was positive, the ninhydrin: positive, on prolonged heating. A complete analysis was carried out.

1.830 mg substance: 0.007 ml N_2 (23°, 748 mm). 1.445 mg substance: 0.258 ml N_2 (23°, 748 mm). 3.010 mg substance: 5.760 mg CO_2; 1.277 mg H_2O. 3.030 mg substance: 5.795 mg CO_2; 1.277 mg H_2O. Found %: N 20.32, 20.36; C 52.23, 52.19; H 4.27, 4.25. $C_{24}H_{24}O_8N_8$. Calculated %: N 20.29; C 52.17; H 4.35.

The substance isolated did not give depression with one obtained from experiment "a".

All aqueous filtrates and water-alcohol filtrates were concentrated to dryness in vacuo. The residue remaining was found to be diketopiperazine. Thus, during the course of this reaction the authors separated phthalide as an intermediate compound, of peculiar hydrazineamidine structure, and also phthalylhydrazide and diketopiperazine as final products. The separation of these substances confirms the proposed structure (V) and permits an assumption as to its decomposition, as per the following scheme:



(V)

To confirm the accuracy of the proposed structure for the above-given compound, the authors arranged the following reactions.

3. Heating of the hydrazide of N,N'-diphthalylglycyldiketopiperazine with absolute alcohol. 0.8 g of the hydrazide of N,N'-diphthalylglycyldiketopiperazine, obtained from the preceding experiment, was placed in a flask with a reflux condenser, and 25 ml of absolute alcohol added. Upon heating to boiling for one hour, a precipitate resulted, which was filtered off after cooling and washed with alcohol. The substance isolated was insoluble in either water or alcohol, but was recrystallized from boiling 50% alcohol. M.p. 340°. From its

properties, it appeared to be the phthalylhydrazide. To the alcoholic filtrate with a basic reaction after concentration in vacuo, there was added absolute alcohol. The resulting substance was filtered off, with protection against moisture of the air (through a calcium chloride tube), was washed with absolute alcohol, and dried over P_2O_5. The substance melted at 200° with decomposition in a sealed capillary, and was readily-soluble in water, alcohol; poorly so in ether. It gave the anhydride reaction and the ninhydrin reaction, as well as a biuret reaction of the tripeptide type, and represented N,N'-diglycyldiketopiperazine (I).

3.180 mg substance: 0.662 ml N_2 (23°, 743 mm). 3.075 mg substance: 4.770 mg CO_2; 1.660 mg H_2O. 3.020 mg substance: 4.700 mg CO_2; 1.550 mg H_2O. 3.020 mg substance: 4.695 mg CO_2; 1.695 mg H_2O. Found %: N 23.94; C 42.30, 42.40, 42.30; H 5.04, 5.75, 6.20; $C_8H_{12}O_4N_4$. Calculated %: N 24.5; C 42.10; H 5.26.

Analysis of this substance clearly indicated its hygroscopicity.

4. Ionophoresis of N,N'-diphthalylglycyldiketopiperazine hydrazide. 0.5 g of the substance was dissolved in aqueous alcohol and subjected for 48 hours to ionophoresis, the cathode solution being changed after 24 hours. After 24 hours the cathodic solution was basic, the anodic acid. The intermedite portion was neutral. After 48 hours the intermedite portion and the anodic portion were completely neutral. Reactions: in the first 24 hours of ionophoresis: a) positive ninhydrin and anhydride reactions in the cathode solution; b) negative ninhydrin and positive anhydride reactions in the middle portion; c) complete absence of any substance in the anode solution.

Analysis of the cathode solution in the second 24 hours of ionophoresis. The cathode solution was basic. The ninhydrin and anhydride reactions were positive. Under the microscope, a drop of the solution after evaporation showed the presence of diketopiperazine. Upon dilution of the middle portion with water, a precipitate separated, which was filtered off and washed with water. By analysis the substance represented phthalyhydrazide.

5. Elimination of the phthalyl group in N,N'-diphthalylglycyldiketopiperazine [9]. The suspension, containing 2.44 g (0.005 mole) of N,N'-diphthalylglycyldiketopiperazine and 10 ml of 1 molar alcoholic hydrazine hydrate solution in 30 ml of absolute alcohol, was heated under reflux for 1 hour. After cooling to room temperature, the precipitate was filtered off and washed with absolute alcohol.

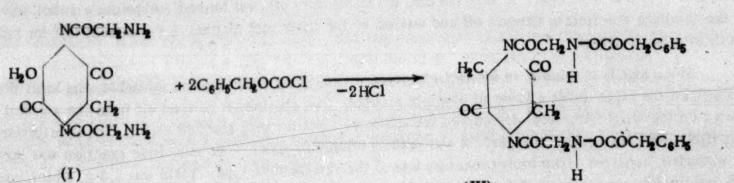
Analysis of the precipitate: did not give the biuret test, but during the course, copper reduction occurred. There should have resulted 1.62 g of phthalylhydrazide from this reaction, by theoretical removal of the phthalyl group, but instead, 2.0 g resulted. The precipitate was therefore treated with 50% alcohol, having placed it on a Büchner funnel. A negligible portion of the precipitate remained insoluble, and from its properties, represented the initial N,N'-diphthalylglycyldiketopiperazine (weight 0.45 g). Upon cooling and concentrating the water-alcohol solution, there was separated in all, 1.25 g of phthalylhydrazide (1.32 g according to theory) which corresponded quantitatively to the removal of the phthalyl group.

Analysis of the alcoholic filtrate. To the filtrate, which gave a basic reaction, absolute ether was added and dry hydrogen chloride passed through to a weak acid reaction. The resulting precipitate was filtered off (with protection from moisture of the air) and was washed with absolute ether. The weight of dried precipitate was 0.8 g, which constituted a 66% yield, calculating on the basis of N,N'-diglycyldiketopiperazine dichloride. It gave the ninhydrin and anhydride reactions, the biuret reaction being of the tripeptide type. It melted above 200°, with decomposition, and represented N,N'-diglycyldiketopiperazine dihydrochloride (II).

Titration according to Sorenson-Gavrilov. 0.0732 g of the substance: 2.4 ml of 0.2 N NaOH (respectively, 4.68 ml of 0.1 N H_2SO_4). Found %: NH_2 8.95. $C_8H_{14}O_4N_4Cl_2$. Calculated %: N 18.6; NH_2 9.3.

Titration according to Willstätter. 0.0467g of the substance: 2.9 ml of 0.1N alcoholic NaOH (respectively, 2.9 ml of 0.1 N H_2SO_4). Found %: NH_2 8.87. $C_8H_{14}O_4N_4Cl_2$. Calculated %: NH_2 9.3.

6. Interaction of N,N'-diglycyldiketopiperazine (I) with carbobenzoxychloride.



(I) (III)

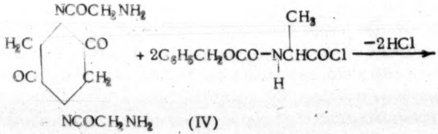
0.3 g of N,N'-diglycyldiketopiperazine was dissolved in 10 ml of water. Simultaneously, 0.41 g (20% excess) of carbobenzoxychloride in ether and 0.1 g of soda in 10 ml of water were added, dropwise, with strong cooling (snow and salt) and with mechanical stirring. The addition lasted for 30 minutes. After completion of the addition and intermixing, stirring was continued for another hour. The aqueous solution was then poured off, and benzene added to the remaining oil. This caused immediate crystallization of the oil, and its transformation to a precipitate which was filtered off and washed with water. The substance was recrystallized from water. The melting point of the dried substance was 110°. Insoluble in water, readily soluble in alcohol and acetone. The ninhydrin reaction was negative, the anhydride reaction positive. Finally a biuret reaction appeared and was of the tripeptide type. From the mother aqueous (neutral) filtrate, the same substance precipitated. Total weight of the substance was 0.4 g, which constituted 81% of theory.

2.365 mg substance: 0.240 ml N_2 (23°, 748 mm). 3.215 mg substance: 0.329 ml N_2 (24°, 742 mm). 3.170 mg substance: 6.735 mg CO_2; 1.440 mg H_2O. 2.415 mg substance: 5.122 mg CO_2; 1.100 mg H_2O. Found %: N 11.51, 11.48; C 57.98, 57.88; H 5.08, 5.09. $C_{24}H_{24}N_4O_8$. Calculated %: N 11.29; C 58.06; H 4.84.

7. Interaction of N,N'-diglycyldiketopiperazine with carbobenzoxyalanylchloride. 0.6 g of N,N'-diglycyldiketopiperazine hydrochloride was dissolved in 10 ml of water and 0.3 g of soda in 10 ml of water was added. Upon strong cooling (snow and salt), and mechanical stirring, 0.96 g of carbobenzoxyalanylchloride in 10 ml of absolute ether was added to the solution, and 0.3 g of soda in 5 ml of water added simultaneously. The addition lasted 30 minutes. After 1 hour of stirring, the ether layer was separated from the aqueous layer in a separatory funnel. The aqueous filtrate was extracted with ether (three times).

Analysis of the water filtrate. The aqueous filtrate was evaporated to dryness in vacuo at 40° on a water bath. Absolute alcohol was added to the residue and once more evaporated to dryness. The precipitate in the flask was transferred to a filter and treated once more with methanol. It was filtered off from the undissolved portion, which was found to be NaCl. Absolute ether was added to the methanol filtrate. The substance which precipitated out was filtered off and washed with absolute ether. The yield was 0.9 g, which constituted 75%, calculating on the basis of the initial hydrochloride salt of N,N'-diglycyldiketopiperazine. The substance melted at 200° with decomposition, and was readily soluble in water; gave a biuret reaction of the tetrapeptide type and a positive anhydride reaction. The ninhydrin reaction was negative. The test for halogen was positive. Repeated reprecipitations from methyl alcohol by ether were of no use. The difficulty in separating the substance from NaCl prompted the authors to repeat the experiment, carrying out the reaction with magnesium oxide instead of soda.

8. Interaction of N,N'-diglycyldiketopiperazine with carbobenzoxyalanylchloride in the presence of magnesium oxide.

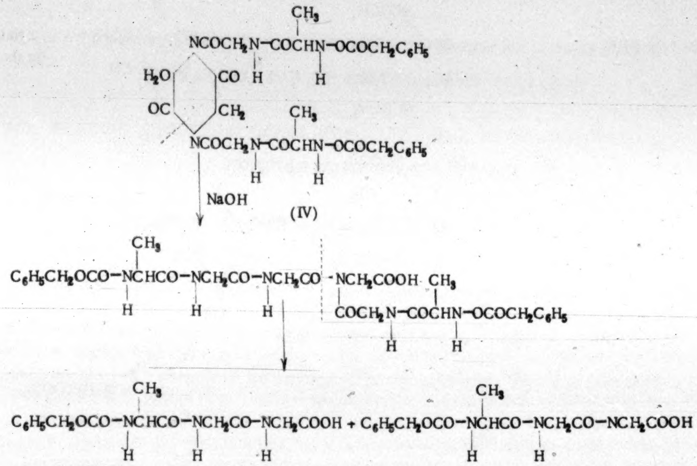


The synthesis of carbobenzoxyalanylchloride was carried out according to Bergmann. The resulting chloroanhydride, in the form of an oil, was treated with petroleum ether and then dissolved in absolute ether. 0.8 g of N,N'-diglycyldiketopiperazine was dissolved in 10 ml of water and 0.3 g of MgO added. 1.28 g of carbobenzoxyalanylchloride in absolute ether was added to the solution, with ice cooling and stirring with a mechanical stirrer. The addition lasted 30 minutes; the solution was continuously stirred for another hour. After termination of the reaction (neutral medium), the precipitate was filtered off and the solution evaporated to dryness in vacuo with heat. A very viscous, but transparent oil, was formed. Absolute alcohol was added to it, the resulting precipitate filtered off and washed on the filter with alcohol; a subsequent test for halogen (Beilstein) was positive.

Since $MgCl_2$ is soluble in alcohol and since the resulting substance was insoluble, the total precipitate was left for the night under a layer of absolute alcohol. The precipitate filtered off from the alcohol was treated on the same filter with dry carbon tetrachloride and then with absolute ether. The precipitate, dried over H_2SO_4, did not contain halogen. It was readily soluble in water. The anhydride reaction was positive, the ninhydrin negative. The biuret reaction was of the tetrapeptide type. Yield was 1.3 g, which constituted 77%, calculating on the basis of initial hydrochloride salt of N,N'-diglycyldiketopiperazine.

6.760 mg substance: 0.0793 ml N_2 (23°, 742 mm). 2.958 mg substance: 6.110 mg CO_2; 1.303 mg H_2O. 2.976 mg substance: 6.144 mg CO_2; 1.300 mg H_2O. Found %: N 13.21; C 56.37, 56.34; H 5.27, 5.18. $C_{30}H_{34}O_{10}N_6$. Calculated %: N 13.17; C 56.43; H 5.33.

Scheme 5



During attempts to carry out the biuret reaction with 2 N-alkali, asymmetric hydrolysis of this compound was observed on the diketopiperazine ring, and with further decomposition of N, N'-carbobenzoxyhexapeptide to 2-carbobenzoxytripeptide. This cleavage was confirmed by a spectrophotometric curve, indicating an equal mixture of tetra- and tri-peptides. As a result, the authors suggest a decomposition scheme for N, N'-dicarbobenzoxyalanylglycyldiketopiperazine under the action of alkali (vide Scheme 5).

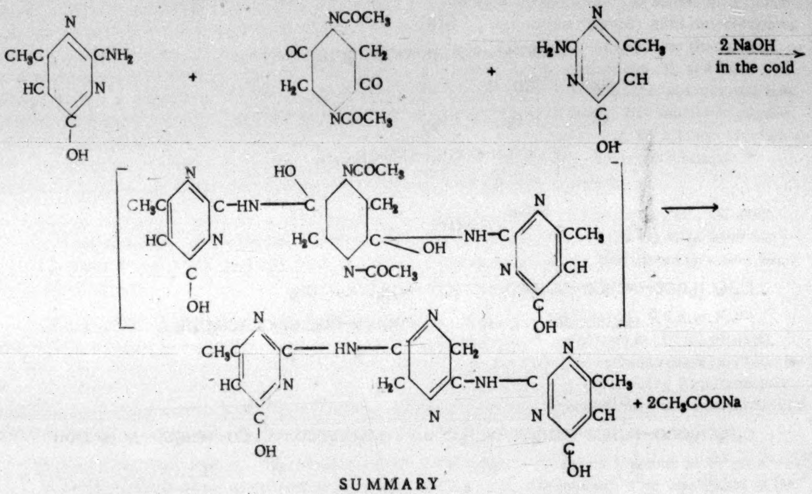
According to the authors' scheme, 2 molecules of protein and 2 diketopiperazines are linked together by 2 tripeptides. The authors have simplified this scheme somewhat, and having utilized the reaction which was discovered between diacetyldiketopiperazine and aminopyrimidines [10] (vide Scheme 6), the authors tried to use the earlier-synthesized N, N'-diglycyldiketopiperazine by combining it with diacetyldiketopiperazine. The reaction proceeded with cleavage of acetic acid, and as the result it was possible to isolate, analyze and characterize the formation of two rings, first the diketopiperazine ring, and second — dihydropyrazine, linked by nitrogens and carbons in positions 2 and 5 to glycine (see Scheme 1, A).

9. Interaction of N, N'-diglycyldiketopiperazine with diacetyldiketopiperazine. Two grams of diacetyldiketopiperazine in 15 ml of alcohol was added to 2.3 g of N, N'-diglycyldiketopiperazine in 20 ml of absolute alcohol. On shaking, everything dissolved. The transparent solution was left standing for 1 hour; a strong odor of the ester, ethyl acetate, was noticed. The medium was basic. Upon passing dry hydrogen chloride into the solution, a precipitate formed, which was filtered off and washed with alcohol. The substance was recrystallized from absolute alcohol. The yield was 3.0 g, which constituted 79% of theory, calculating on the basis of N, N'-diglycyldiketopiperazine taken for reaction. Soluble in water with heating; insoluble in alcohols, gave a positive anhydride reaction, and a biuret reaction of the tripeptide type; ninhydrin reaction was positive upon prolonged heating. M.p. 226°, with decomposition.

1.830 mg substance: 0.346 ml N_2 (23°, 743 mm). 3.211 mg substance: 4.458 mg CO_2; 1.280 mg H_2O. 3.117 mg substance: 4.344 mg CO_2; 1.277 mg H_2O. Found %: N 22.06; C 37.89, 38.03; H 4.13, 4.17. $C_{12}H_{16}N_6O_4Cl_2$. Calculated %: N 22.17; C 38.00; H 4.22.

The compound obtained (see Scheme 1, A) as yet is not the simplified model, No. 2, for the protein structure, but already permits the planning of another method of synthesis of quite a labile structure, which may for a moment exist as a structural fragment of the protein.

Scheme 6



SUMMARY

1. The feasibility of eliminating the phthalyl group in 1,4-diphthalylglycyl-2,5-diketopiperazine by the hydrazine method, with formation of N,N'-diglycyldiketopiperazine, has been demonstrated.

2. An intermediate compound (V) has been isolated.

3. N,N'-Diglycyldiketopiperazine (I), its hydrochloride salt (II), and the carbobenzoxyderivative (III) have been synthesized.

4. The carbobenzoxy derivative of N,N'-diglycylalanine (IV) has been obtained.

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* See Consultants Bureau English translation, page 2219, ff.

** See Consultants Bureau English translation, page 1673 ff.

SPECTROPHOTOMETRY OF BIURET COMPLEXES AS A METHOD OF INVESTIGATION OF PROTEINS AND PEPTIDES

XVI. RELATIVE ACTIVITIES OF COPPER, NICKEL AND COBALT IN THE FORMATION OF THE TRIPEPTIDE BIURET COMPLEX (GLYCYL)

M. I. Plekhan and E. N. Voluiskaya

The biuret complexes of the polypeptides with various metals (copper, nickel and cobalt) represent groups of compounds, each possessing peculiarities. The distinction between one type of complex and the other, and within the range of each group, is displayed with an obvious variability. In a series of copper biuret complexes, the transition from one type of complex to the next is quite evident, but the clearest is found to be the transition from the violet complex of the tripeptide to the red complex of the tetrapeptide (and vice versa [1,2,3]). This transition is marked by a shifting of the absorption maximum, with an increase in absorption intensity in the short wave range, and with a considerable decrease in absorption in the long wave range. For a series of nickel complexes [4], transition from the orange complex of the tripeptide to the canary yellow complex of the tetrapeptide is manifested chiefly by a decrease in the absorption intensity in the range 600-730 millimicrons, which is not so clearly evident at low concentrations. However, the transition from the orange complex of tripeptide to the blue complex of the dipeptide is so clearly evident that it can serve as an indicator for the appearance of dipeptides in the solution.

For the group of cobalt complexes [4], the most intensive application, in a practical sense, is found to be that contrast which gives a reaction of the cobalt complex of the dipeptide, and the absence of reaction with amino acids.

Thus the use of various metals in the biuret reaction has definite advantages, since it permits utilization of the most characteristic peculiarities for each group of complexes. In the first stages of decomposition, as a study of enzymatic, acid and alkaline hydrolysis by the authors has indicated, dipeptides do not appear, but rather formation of chains longer than tripeptides proceeds, with a correlation in changes from violet to red; therefore, in the early stages of decomposition, of greatest interest is perhaps the application of the biuret reaction with copper.

After 1-1.5 hours of acid and of alkaline hydrolysis of gelatin, the appearance of dipeptides was observed, the quantity of which increased within a period of 30 hours. At this stage of decomposition, the use of nickel complexes was found to be especially valuable. In the same cases of hydrolysis, where complete decomposition to the amino acids is required, use of the reaction with cobalt should be an accurate indicator of termination of the reaction.

The question naturally arises whether a simultaneous biuret reaction course with several metals, or a reaction course with one of the metals in the presence of the already-formed complex of another metal, would be possible. A prerequisite condition for this is found to be: a difference in the formation activity of the biuret complex with various metals; a difference in which it would be possible to arrange copper, nickel and cobalt in a given sequence of increasing activity; a sequence in which one metal would be able to displace another (metal) from the complex under any conditions.

The authors have tried to determine experimentally whether such a phenomenon in reality does occur. Experiments on the relative activity of biuret complex formation for the glycyl tripeptide with copper, nickel and cobalt were carried out.

Experiment 1 (Cu + Ni + Co). A solution of the copper biuret complex of glycyl tripeptide was obtained (0.0032 M), the spectrophotometric curve * of which is given in Fig. 1 (Curve I).

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* Spectrophotometry was carried out in a König-Martens machine.

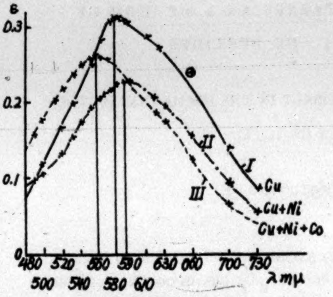

Fig. 1. Spectrophotometric curves for mutual displacement of Cu, Ni and Co in the biuret complexes of the tripeptide (0,0032 M).

3 ml of 0.21 M nickel sulfate was added to 13 ml of a solution of the copper biuret complex. After 1.5 hours, a spectrophotometric curve was taken, II (Fig.1), (the color of the solution being dark violet). 2 ml of 0.24 M cobalt sulfate solution was then added to 10 ml of the Cu + Ni biuret complex. After 2 hours, Curve III (Fig. 1) was taken. This experiment showed that the appearance of nickel in a solution where the copper complex exists leads to a decrease in the absorption intensity over the entire range of the spectrum from 480 to 730 millimicrons. A very strongly depressed absorption was noted in the wave length range 560-600 millimicrons. The position of the absorption maximum was shifted toward the long waves, and stopped at 590 millimicrons. These changes attest to the fact that nickel partially supplants copper in the complex. A mixture of two complexes is formed — of the copper and nickel complexes. The addition of cobalt to this mixed solution led to a considerable increase of absorption for wave lengths 480-590 millimicrons, i.e., on the very section of the wave length where the cobalt complex possesses the maximum absorption intensity. The position of the maximum was shifted toward the short waves and stopped at wave length 560 millimicrons. Cobalt supplanted one of the metals in the complex. Thus in the solution resulted a mixture of all three complexes. In the sequence of appearance in solution of Cu + Ni + Co, neither nickel nor cobalt were able completely to supplant copper, nor each other.

Experiment 2 (Ni + Co + Cu). A 0.24 M solution of $CoSO_4$ was added to the orange solution of tripeptide biuret complex (Fig. 2, Curve I). After two hours, Curve II (Fig. 2) was taken. A change in the character of absorption occurred, which indicated that cobalt partially supplants nickel in the complex. A mixture of the nickel and cobalt complexes resulted. Cupric hydroxide was added to this mixture and after 1 hour, Curve III was taken, which showed that copper very strongly supplants both nickel and cobalt. Curve III, on the whole, resembles the curve for the copper biuret complex of the tripeptide. Only the existence of a considerably higher absorption in the short wave lengths, instead of the long wave lengths, suggested that any cobalt complex, and also possibly nickel complex, were present in the solution. In the sequence Ni + Co + Cu, the predominant, but not complete, activity belongs to copper.

Experiment 3 (Co + Ni + Cu). The red-brown solution of cobalt biuret complex of the tripeptide (Fig. 3, Curve I) was mixed with nickel hydroxide. Curve II (Fig. 3) indicated that nickel displaced cobalt but very little. The addition of copper to this solution, likewise, showed negligible effect. In Fig. 3 (Curve III) it can be seen that absorption in the wave length range 530 to 730 millimicrons increases but little. Copper partially supplants cobalt. But as a whole, the curve preserves its outline inherent for the cobalt complex of the tripeptide. This experiment indicates that in the sequence Co + Ni + Cu, the cobalt complex possesses the greatest stability. Apparently the ability of a metal to form a stable complex is a property to which is not imparted a simultaneous ability to displace another metal from its complex.

In Experiment 1 copper displays an ability to form quite a stable complex, and in Experiment 2 quite a high activity as compared with Ni and Co, but in the 3rd Experiment copper has negligible ability for displacing Co. Nevertheless, on the basis of these experiments it can be concluded that the activity of complex formation and the stability of the complex is lowest for nickel. Although none of the metals display absolute predominant activity of complex formation, none-the-less, they can be arranged in a decreasing order as follows: copper ⟶ cobalt ⟶ nickel. (There is negligible displacement of copper by nickel and cobalt, cobalt is practically unreplaced by nickel or copper, and nickel is completely replaced by copper, but only negligibly so by cobalt).

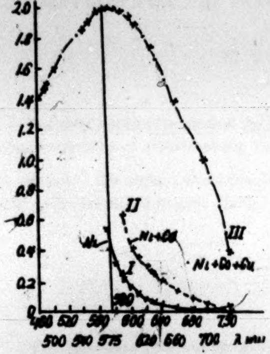

Fig. 2. Spectrophotometric curves for mutual displacement of Ni, Co and Cu in the biuret complexes of the tripeptide (0.032 M).

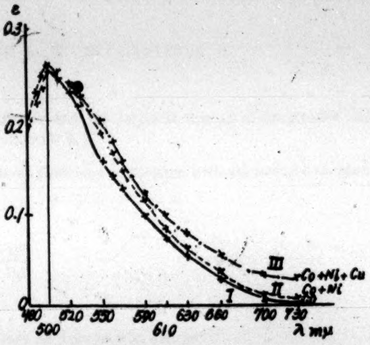

Fig. 3. Spectrophotometric curves of mutual replacement of Co, Ni and Cu in the biuret complex of tripeptide (0.0014 M).

These data do not coincide with the observations of Iesserer [5,6] who analytically studied the stability of Cu, Ni and Co casein complexes, and who found that nickel and cobalt displace copper. Copper itself, in his opinion, was unable to displace either nickel or cobalt.

SUMMARY

The simultaneous introduction of several metals into the biuret reaction complicates the picture of complex formation; therefore, application of the biuret reaction with various metals is best carried out only by separate tests with each metal.

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* See Consultants Bureau translation, p. 341, 347, 635, 641.

** See Consultants Bureau translation, p. 1675.

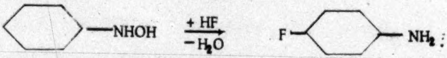
*** See Consultants Bureau translation, p. 2181.

A NEW METHOD FOR THE INTRODUCTION OF FLUORINE INTO THE AROMATIC RING

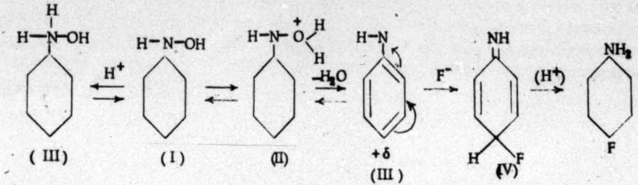
A. I. Titov and A. N. Baryshnikova

The only applicable method for introducing fluorine into the aromatic ring up to the present time has been decomposition of aryldiazonium fluoride or borofluoride [1].

Recently the authors found that the interaction of phenylhydroxylamine with anhydrous hydrogen fluoride produces p-fluoroaniline in good yield:



The mechanism for this discovered reaction may be presented as follows:



Arylhydroxylamine (I) in hydrogen fluoride forms an ammonium cation (II') or oxonium cation (II). The latter, under the influence of strong acid, splits water and converts into the anhydro-cation (III). Due to the presence on the p-carbon of this cation with a +δ charge, it adds the fluoride ion and forms a quinoid product (IV), whose prototropic transformation leads to formation of p-fluoroaniline.

The mechanism so presented very readily explains the various transformations of arylhydroxylamines under the influence of acids when a third component—amine, alcohol, or other substances [2] is involved in the reaction. The data obtained by the authors in their experiments prompted them to adopt an intermolecular character of arylhydroxylamine regrouping, and to reject the generally accepted, up to the present time, interpretation of these reactions as being intramolecular processes [3].

Description of the Experiment

8 g of phenylhydroxylamine, in small portions, was introduced at 0° into 35 ml of anhydrous hydrogen fluoride placed in a copper crucible. After standing for 2 days at +10°, the reaction mass was poured into potash solution and the mixture steam distilled. The distillate fraction was saturated with salt and extracted with ether. After drying the extract and distilling the ether off, 3.8 g of oil remained, which distilled at about 86° under 20 mm pressure; specific gravity of the distillate fraction at 20° was 1.156. These constants corresponded to the literature data for the properties of p-fluoroaniline. Heating 0.3 g of the amine with 0.6 g of acetic anhydride, with subsequent water treatment, gave 0.41 g of the acetyl derivative, melting at 143-145°. A single recrystallization from alcohol gave p-fluoroacetanilide, with m.p. 150.5°, which coincided with the literature data for this product; upon heating its mixed sample with known p-fluoroacetanilide, no m.p. depression was observed.

SUMMARY

A new method for introducing fluorine into the aromatic ring, using the conversion of phenylhydroxylamine to p-fluoroaniline in anhydrous hydrogen fluoride as an example, has been discovered. A reaction mechanism has been given.

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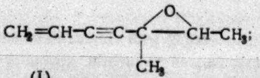
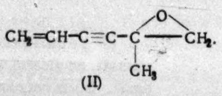
THE INTERACTION OF α-OXIDES OF THE VINYLACETYLENE SERIES WITH OXYGEN-CONTAINING AND WITH ORGANOMAGNESIUM COMPOUNDS. III

F. Ya. Perveev and N. I. Kudryashova

Despite the many investigations in the field of study of olefin oxide interaction with organomagnesium compounds, there has been little study with regard to the position at which the oxide ring is broken as related to structural features of the molecules. To clarify this problem, the authors have investigated interaction of organomagnesium compounds with oxides of the vinylacetylene series. As the objects of investigation, 3-methyloxido-2,3-hepten-6-yne-4 (I) and 2-methyloxido-1,2-hexen-5-yne-3 (II) were selected:



(I)



(II)

The vinylacetylene alcohols were synthesized in the usual manner. An ether solution of the oxide was gradually added to an ether solution of the organomagnesium compound with strong cooling (ice and salt) and stirring. During the interaction of ethylmagnesium bromide with 3-methyloxido-2,3-hepten-6-yne-4 (I), an alcohol was isolated in 54% yield – a mobile liquid of pleasant odor, which, in the absence of antioxidants, became viscous upon standing in air, and then transformed into a glassy mass. One of three possible isomeric alcohols might have been expected:

(III) $CH_2{=}CH{-}C{\equiv}C{-}C(CH_3)(OH)CH(CH_3)C_2H_5$,

(IV) $CH_2{=}CH{-}C{\equiv}C{-}C(CH_3)(C_2H_5)CHOH{-}CH_3$,

(V) $CH_2{=}CH{-}C{\equiv}C{-}CH(CH_3)C(CH_3)(OH)C_2H_5$.

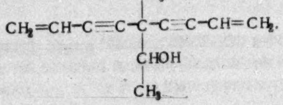
The last alcohol might have formed as a result of preliminary isomerization of the oxide to the ketone under the conditions of the synthesis.

In order to determine the resulting structure, the product was isomerized in the presence of mercury sulfate in methanol solution [1]. After processing of the reaction mixture, the initial product was isolated. It is known [2] that during the isomerization of secondary α-vinylethynylcarbinols, saturated dialkoxyketones result, and upon isomerization of tertiary α-vinylethynyl carbinols, unsaturated monoalkoxyketones predominate.

No neutral products were found during oxidation by $KMnO_4$ in the cold, nor after boiling of the acidified solution of obtained substance. This indicated the absence of α-hydroxyacid, which could have formed during oxidation of the alcohol (III). Among the oxidation products, oxalic acid in the form of the Ca-salt of the acid, corresponding to the composition $C_7H_{14}O_3$, was found. On the basis of these data, the authors have assigned the structure (IV) to the product synthesized.

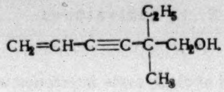
Upon condensing the oxide (I) with vinylacetylenemagnesium bromide, an alcohol was synthesized, consisting of a colorless, mobile liquid, with b.p. 103-104° at 6 mm. The crude product explodes upon heating above 140°. (Distillation was carried out in small lots.) The purified substance was found to be a relatively stable compound. Upon storage in air it becomes yellow after several days. The alcohol remains unchanged, except for negligible resinification, upon treating with 50% H_2SO_4. Upon hydrogenating in alcoholic solution over Raney Ni, a theoretical volume of hydrogen was absorbed (calculating for two double and two triple bonds) with the formation of a saturated alcohol with b.p. 95-96° at 6 mm. The authors were unable fully to determine the structure by ozonization and oxidation; however, the stability with regards to H_2SO_4 indicated the secondary character of the alcohol (VI):

(VI)



$$CH_2{=}CH{-}C{\equiv}C{-}\overset{CH_3}{\underset{\underset{CH_3}{CHOH}}{C}}{-}C{\equiv}C{-}CH{=}CH_2$$

Upon interacting ethylmagnesium bromide with 2-methyloxido-1,2-hexen-5-yne-3 (II), an alcohol with b.p. 72-73° at 4 mm was isolated – a colorless mobile liquid. It gradually polymerized upon storage in air. In methanol, with mercury sulfate present, it did not isomerize. The Ca-salt of the acid, composition $C_6H_{12}O_3$, was separated among the oxidation products. Thus, on the basis of the data obtained, the authors gave the structure (VII) to the compound synthesized:

(VII) 

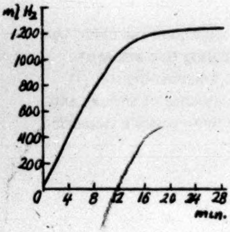
$$CH_2{=}CH{-}C{\equiv}C{-}\overset{C_2H_5}{\underset{CH_3}{C}}{-}CH_2OH$$

The absence of secondary β-vinylacetylene alcohol also

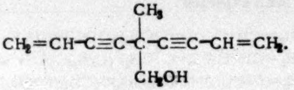
$$(CH_2{=}CH{-}C{\equiv}C{-}CH(CH_3)CHOH{-}C_2H_5)$$

indicated the fact that the isomerization product of the given oxide does not react with organomagnesium compounds.

By condensing the oxide (II) with vinylacetylenemagnesium bromide, an alcohol was synthesized – a mobile, gradually-polymerizing liquid. It was not changed by treatment with 50% H_2SO_4. Thermally unstable. Exploded upon heating above 140°. Was fully hydrogenated over Raney nickel in alcoholic solution. The hydrogenation curve is given.



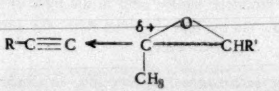
The authors have assumed structure (VIII) for the synthesized alcohol.

(VIII) 

$$CH_2{=}CH{-}C{\equiv}C{-}\overset{CH_3}{\underset{CH_2OH}{C}}{-}C{\equiv}C{-}CH{=}CH_2.$$

Thus it has been established that during interaction of asymmetrically-disubstituted and trisubstituted oxides of the vinylacetylene series with organomagnesium compounds, primary and secondary alcohols are respectively formed, i.e., rupture of the oxide ring occurs at that carbon which is directly adjacent to the triple bond, while the olefin oxides of similar structure [3] give, respectively, secondary and tertiary alcohols, i.e., rupture of the oxide ring occurs at the more hydrogenated carbon atom.

This difference in rupture of the oxide ring is explained by the fact that rupture of the oxide ring occurs under the action of organomagnesium compounds at the more positively-charged carbon atom. Just as the triple bond has the ability to attract electrons to itself, in a manner similar to that of the carbonyl groups, so there is always produced at the α-carbon atom of the oxide a more positive charge.



EXPERIMENTAL

1. Synthesis of 3-methyl-3-ethyl-hepten-6-yne-4-ol-2 (IV). 30 g of the oxide (I), diluted with a triple volume of absolute ether, was gradually added to an ether solution of ethylmagnesium bromide. The reaction flask was cooled (ice and salt). The yield of alcohol is decreased when cooling is inadequate. After all of the oxide was added, the reaction mixture was left overnight. The organomagnesium complex was then decomposed with a 30% solution of acetic acid. The ether solution was separated, the aqueous – treated twice with ether. The ether extracts were dried with Na_2SO_4. The ether was distilled off and the remaing product redistilled in vacuo. After a triple distillation, 20 g (54%) of the alcohol, with b.p. 81-82° at 10 mm, resulted; d_4^0 0.9216; d_4^{18} 0.9002; n_D^{18} 1.4824; MR_D 48.23, calculated 47.44.

0.0765, 0.0944 g substance: 0.2206, 0.2715 g CO_2; 0.0727, 0.0897 g H_2O. 0.1448, 0.1227 g substance: 24.3, 20.1 ml CH_4 (19°, 766.0 mm). Found %: C 78.68, 78.75; H 10.63, 10.68; active H 0.681, 0.681. $C_{10}H_{16}O$. Calculated %: C 78.89; H 10.59; active H 0.662.

Oxidation of the alcohol (IV). This was carried out in the cold with 3% $KMnO_4$ solution. 9.4 g of the substance was taken and 48.5 g of $KMnO_4$ was used for the oxidation. The MnO_2 was filtered off and washed with hot water. A portion of the solution was distilled off from the filtrate, in which neutral substances were not found. The remaining solution was then evaporated to a small volume, acidified with 10% H_2SO_4, and boiled under reflux. With further treatment, neutral substances and volatile substances were not found. Among the non-volatile substances, oxalic acid, with m.p. 182° was isolated (mixed sample did not give depression) and an hydroxyacid of the composition $C_7H_{14}O_3$, which was isolated as follows: the basic solution, after removal of the volatile acids by distillation, was treated with ether, the ether evaporated and to the remaining oily product, 15 g of calcium carbonate and 50 ml of water added. The mixture was boiled under reflux for 2 hours. The precipitate was filtered off and washed several times with water. The filtrate was evaporated in vacuo. The remaining viscous mass was placed in a vacuum desiccator. The resulting slightly-yellow powder was dried to constant weight at 105-110°, and was calcined.

0.0876 g substance: 0.0140 g CaO. Found %: Ca 11.5. $(C_7H_{13}O_3)_2Ca$. Calculated %: Ca 12.1.

2. Synthesis of 2-methyl-2-ethylhexen-5-yne-3-ol-1 (VII). 17 g of the substance (66.5%), with b.p. 72-73° at 4 mm was obtained from 20 g of the oxide (II); d_4^{20} 0.9041; n_D^{20} 1.4889; MR_D 44.1; calculated 42.9.

0.1146, 0.0979 g substance: 0.3323, 0.2798 g CO_2; 0.1063, 0.0901 g H_2O. 0.1487, 0.1369 g substance: 26.02, 23.82 ml CH_4 (18°, 773 mm). Found %: C 78.05, 78.00; H 10.38, 10.30; active H 0.738, 0.734. $C_9H_{14}O$. Calculated %: C 78.21; H 10.21; active H 0.729.

Oxidation of alcohol (VII). This was carried out by the above-indicated procedure. 5.5 g of the substance was taken, and 33 g of $KMnO_4$ was used for the oxidation. No neutral products were found, nor any volatile acid among the oxidation products. An hydroxyacid of composition $C_8H_{12}O_3$ was found.

0.1272 g substance: 0.0230 g CaO. Found %: Ca 12.92. $(C_8H_{11}O_3)_2Ca$. Calculated %: Ca 13.17.

3. Synthesis of alcohol (VI). 40 g of dry vinylacetylene was passed into an ether solution of ethylmagnesium bromide. The reaction mixture was left for the night. Then, with cooling (ice and salt), 34 g of the oxide, diluted with a triple volume of absolute ether, was added dropwise. A strong resinification was observed. After all of the oxide had been added, stirring was continued for another 3 hours. The resulting organomagnesium complex was decomposed with 30% acetic acid solution. The ether layer was separated, and washed with water; the aqueous layer –treated three times with ether. The ether extracts were added to the basic solution and dried over Na_2SO_4. The ether was distilled off, and the remaining product redistilled in vacuo. 20 g of the alcohol, with b.p. 103-104° at 6 mm, was isolated; d_4^0 0.9597; d_4^{21} 0.9399; n_D^{21} 1.5225; MR_D 56.6; calculated 54.2.

0.1461, 0.0930 g substance: 0.4576, 0.2821 g CO_2; 0.1085, 0.0693 g H_2O. 0.0922, 0.1153 g substance: 13.3, 15.9 ml CH_4 (17.5°, 755.8 mm). Found %: C 82.67, 82.71; H 8.30, 8.33; active H 0.596, 0.596. $C_{12}H_{14}O$. Calculated %: C 82.83; H 8.11; active H 0.578.

Hydrogenation of alcohol (VI) was carried out over Raney Ni in absolute alcohol. 10.5 g of the substance was taken. 8.2 liters of hydrogen was used. The calculated volume was 8.1 liters. After completion of the hydrogenation, the catalyst was filtered off and the ethyl alcohol distilled in vacuo. The remaining product redistilled at a temperature of 107-108° at 10 mm. There resulted a colorless liquid with faint odor; d_4^0 0.8609; d_4^{17} 0.8458; n_D^{17} 1.4471; MR_D 58.9; calculated 59.1.

0.0925, 0.1018 g substance: 11.9, 13.0 ml CH_4 (20°, 754 mm). Found %: active H 0.524, 0.520. $C_{12}H_{26}O$. Calculated %: active H 0.541.

4. Synthesis of alcohol (VIII). 40 g of the oxide (II) was taken. 23 g of the substance, with b.p. 109-110° at 8 mm resulted. The alcohol consisted of a colorless liquid which turned yellow on standing. d_4^0 0.9668; d_4^{20} 0.9476; n_D^{20} 1.5292; MR_D 52.09; calculated 49.58.

0.0799, 0.0836 g substance: 0.2410, 0.2526 g CO_2; 0.0553, 0.0563 g H_2O. 0.0830, 0.1136 g substance: 13.3, 17.6 ml CH_4 (21°, 753 mm). Found %: C 82.26, 82.39; H 7.65, 7.53; active H 0.645, 0.627. $C_{11}H_{12}O$. Calculated %: C 82.5; H 7.5; active H 0.630.

Hydrogenation of alcohol (VIII). This was carried out over Raney Ni in absolute alcohol. 3.5 g of substance was taken. 3052 ml of hydrogen was used for the hydrogenation (19°, 767 mm). The calculated volume of hydrogen was 2940 ml. A substance with b.p. 95° to 96° at 7 mm resulted – a colorless liquid with faint odor; d_4^{20} 0.8427; n_D^{20} 1.440; MR_D 53.8; calculated 54.5.

0.0920, 0.0986 g substance: 14.3, 13.9 ml CH_4 (19°, 752 mm). Found %: active H 0.635, 0.575. $C_{11}H_{24}O$. Calculated %: active H 0.586.

SUMMARY

1. Upon interacting ethylmagnesium bromide with 3-methyloxido-2,3-hepten-6-yne-4 (I), and 2-methyloxido-1,2-hexen-5-yne-3 (II), the alcohols: 3-methyl-3-ethylhepten-6-yne-4-ol-2 (IV) and 2-methyl-2-ethylhexen-5-yne-3-ol-1 (VII) have been isolated and characterized.

2. It has been determined that rupture of the oxide ring under the action of organomagnesium compounds occurs at the α-carbon.

3. A method for synthesis of primary and secondary β-vinylacetylene alcohols has been developed.

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PHYSICO-CHEMICAL INVESTIGATION OF SYSTEMS CONTAINING HALIDES OF IODINE AND HALIDES OF OTHER ELEMENTS

X. THE SYSTEMS $IBr-KBr$ AND $IBr-AlBr_3$

Ya. A. Fialkov and O. I. Shor

In respect of physical and chemical properties the halides of iodine resemble on the one hand free halogens – as had already been noted by D. I. Mendeleev [1] – and on the other hand polar salt-forming halides. * This is true of iodine chloride and iodine bromide.

These iodine halides possess very low polarity in the free state; thus, Luft [3] gives the dipole moment of ICl as 0.5; but in nonpolar solvents (CCl_4 and cyclohexane) it rises to 1.49 and 1.47 [4]. The dipole moment of IBr in bromine solution ** is equal to 1.21 D (I.A. Sheka [5]). In the same paper Sheka showed that the character of the bond in iodine bromide changes with the medium.

Consequently, there are grounds for assuming that ICl and IBr can behave in chemical reactions not only like halogens but also like polar halides. Polarity is developed, for instance, when ICl and IBr react with halides of various elements.

The results of the investigations described in previous communications showed that complex compounds of ICl and IBr with halides of a series of other elements vary in structure in dependence on the polarity and structure of those halides. Thus, the complexes of PCl_5 or PBr_5 with ICl and IBr respectively, possess a structure expressed by the general formula $[PX_4][IX_2]$, where X = Cl or Br [6, 7]. Similar complex anions are characteristic of complexes of the $KX \cdot IX$ type [8, 9, 10].

Whereas iodine is the cation in products of addition of iodine chloride to $SbCl_5$ or $SbCl_3$ ($SbCl_5 \cdot 2ICl$ and $SbCl_5 \cdot 3ICl$ or $SbCl_3 \cdot 5ICl$ and $SbCl_3 \cdot 4ICl$), antimony and chlorine enter into the composition of the complex anion [11]. Analogous conclusions can be arrived at in respect of complex compounds of ICl with aluminum chloride; the structure $I[AlCl_4]$ is attributed to the simplest of these, $ICl \cdot AlCl_3$ by Fialkov, and Kaganskaya [8] and by Shor [10].

In view of the results of these investigations, it was a matter of great interest to continue them in the direction of reaction of iodine chloride and iodine bromide both with the highly polar potassium halides and with the nonpolar aluminum chloride and bromide. Among systems of this type the systems ICl-KCl and $ICl-AlCl_3$ have been studied in fair detail [8, 10, 12] in the absence of an organic solvent and in nitrobenzene solutions. The analogous systems IBr-KBr and $IBr-AlBr_3$ have been studied chiefly in nitrobenzene [9], by the methods of electric conductivity measurement, cryoscopy and ion transfer where a great similarity was revealed in the properties of both groups of systems (with chlorides or bromides).

Evidence of formation of complexes in the systems $KX-IX-C_6H_5NO_2$ (where X = Cl or Br) is provided by the following facts: a) Potassium halides are insoluble in nitrobenzene but dissolve in it in presence of ICl or IBr; the solutions are good electric conductors, the conductivity of the system $KBr-IBr-C_6H_5NO_2$ being of the same order ($10^{-3}ohm^{-1}cm^{-1}$) as that of the system $KCl-ICl-C_6H_5NO_2$ but slightly lower; b) when KCl or KBr dissolves in nitrobenzene solutions of ICl or IBr, the freezing point depression is not only not increased but is even decreased. This signifies that the complexes formed in these systems undergo association; this effect is particularly marked in systems containing bromides.

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* The literature on this problem was discussed in the first paper [2].

** Iodine bromide does not form a compound with bromine.

Ion transfer studies showed that potassium migrates to the cathode, while iodine and chlorine or iodine and bromine – in the form of a complex anion – move to the anode. On the basis of the qualitative characteristics of these processes, the formula $K[IX_2]$ can be attributed to these complexes [9]. Complexes of this composition $KICl_2$ and $KIBr_2$, were obtained in an investigation of the system KCl-ICl by the solubility method [13] and by a preparative method [14].

The electric conductivity of the binary systems KCl-ICl and $AlCl_3$-ICl is somewhat higher than that of these systems dissolved in nitrobenzene when the molar ratio is the same. A definite effect on the electric conductivity of nitrobenzene solutions of these systems is possibly exercised by the association of the resultant complexes.

Data from electric conductivity measurements, cryoscopic examination and study of ion transfer demonstrate the formation of complexes in the systems IX-AlX_3-$C_6H_5NO_2$.

Only one complex, $2ICl \cdot AlCl_3$, is revealed on the melting diagram of the system ICl-$AlCl_3$ [10]. Bearing in mind, however, the instability of this complex and the phenomena observed during a study of the system ICl-$SbCl_3$ [11], it is impossible to exclude the possibility of existence of $ICl \cdot AlCl_3$ in the liquid phase and in nitrobenzene solutions, due to partial dissociation; products of more complicated structure may also be formed due, for example, to further solvation with iodine chloride.

A study of ion transfer, of great interest for the clarification of this problem, showed that the systems ICl-$AlCl_3$ and ICl-$AlCl_3$-$C_6H_5NO_2$ exhibit some differences in this connection: Migration of iodine to the cathode is observed in the first of these systems, while aluminum and chlorine migrate to the anode [10]; in a nitrobenzene solution of ICl-$AlCl_3$, however, the anolyte was found to have a higher content of aluminum and chlorine as well as of iodine [8]. The influence of the solvent on the process of electrolysis of this and of analogous systems is discussed in the next communication.

For the purpose of elucidation of the composition and nature of the complexes formed by reaction of iodine halides with potassium or aluminum halides, it was also important to compare similar systems containing ICl and chlorides or IBr and bromides of these metals.

Systems of this type, however, containing iodine bromide, have hitherto been inadequately investigated. The electric conductivity of solutions of KBr in liquid IBr has been measured at 45° and 55° [2]. It was of the same order ($10^{-2} ohm^{-1} cm^{-1}$) as the electric conductivity of the system KCl-ICl (but slightly higher) at the same temperature [10]*, although the electric conductivity of ICl itself at 45° is nearly ten times higher than that of IBr at 45°. The electric conductivity of both systems increases with rising concentration of KCl or KBr.

The electric conductivity isotherms of the systems IBr-$AlBr_3$ [2] and ICl-$AlCl_3$ [10] exhibit the same dependence on concentration with a maximum in the region of approximately 10-12 mole % AlX_3. The first of these systems conducts current more weakly (conductivity at 45° is approximately $10^{-4}-10^{-3} ohm^{-1} cm^{-1}$) than the second ($10^{-3} ohm^{-1} cm^{-1}$).

The viscosity of the system IBr-$AlBr_3$ has also been measured at 100° [2]. It was necessary to perform measurements at such a relatively high temperature in order to cover the whole region of concentrations from 0 to 100% **.

The viscosity isotherm has a maximum at a concentration of about 54 mole % $AlBr_3$, very close to the maximum on the molecular electroconductivity curve (at 100°), calculated on IBr as the electrolyte [2]. Consequently, the viscosity measurements at 100° have established the existence of a complex with an equimolar composition.

On the basis of these facts we can assume that at lower temperatures complexes of more complicated composition might be formed. With the aim of confirming this conjecture, it was decided to perform the thermal analysis of the system IBr-$AlBr_3$.

Furthermore, the transfer of ions in the systems IBr-$AlBr_3$ and IBr-KBr was studied with the objective of clarifying the problems discussed above.

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[*] Due to the relative low solubility of KBr in iodine bromide, measurements could only be performed up to concentrations of approximately 8 mole % KBr.

[**] See Table 2 for results of thermal analysis of this system.

EXPERIMENTAL

The preparation and purification of the materials and the methods of investigation have been described in the previous communications.

1. System IBr–KBr. Electrolysis and Transfer of Ions.

As was pointed out above, the limited solubility of KBr in fused IBr necessitated the preparation for these experiments of melts containing only 8.4–9.7 mole % KBr. Electrolysis was carried out in a small U-shaped vessel with platinum electrodes in a water thermostat at 40-45°. The current strength was approximately 40 mA. Duration of an experiment 3-4 hours. A dark-grey iodine precipitate was observed to form at the cathode. After the cathode had been washed with anhydrous ether, there remained a crumbly precipitate readily soluble in water to form a solution with a strongly alkaline reaction containing ions of potassium and bromine. A similar phenomenon was observed in the electrolysis of the system ICl–KCl [10].[*]

Ion transfer experiments were performed in a vessel with platinum electrodes. Current strength 10-12 mA; duration of experiments 22-26 hours at 40-45° (in a water thermostat). At the close of the experiments the liquid from each compartment of the vessel was poured into weighed flasks fitted with ground-glass stoppers.

In order to avoid loss of iodine and bromine during treatment of the electrolyte with a saturated aqueous solution of SO_2 due to the resultant strongly exothermic reaction, the weighed liquids were dissolved in nitrobenzene, after which the SO_2 solution was introduced. The analytical procedure was as for the system ICl–KCl except that the iodine was determined in presence of bromine by a modified Winkler method [15].[**]

The experimental data for ionic transfer are presented in Table 1 which shows that the potassium content increases in the cathodic section and the bromine content in the anodic section. The iodine content increases in the catholyte but to a relatively small extent.

TABLE 1
Ion Transfer in the System IBr–KBr

No. of Expt.	Comp. of test solution (in mole % KBr)	Amount of copper separated in coulometer (in g)	Substance being determined	Solution after electrolysis				Transfer No.		No. of transferred milli-equivalents
				Cathode section		Anode section				
				Required (g)	Found (g)	Required (g)	Found (g)	Catholyte	Anolyte	
1	9.70	0.1842	K	0.2147	0.3111	0.1714	0.0748	0.43	0.43	2.47
			I	6.4720	6.5943	5.1664	5.0419	0.17	0.17	0.96
			Br	4.5154	3.8142	3.6045	4.2997	1.51	1.50	8.69
2	8.41	0.1955	K	0.1911	0.2907	0.1680	0.0683	0.42	0.42	2.55
			I	6.6818	6.8203	5.8735	5.7343	0.18	0.18	1.09
			Br	4.6008	3.8721	4.0414	4.7592	1.48	1.46	8.97

When analyzing these data we must remember that the investigated system IBr–KBr contained a considerable excess of IBr (just as the system ICl–KCl contained a considerable excess of ICl). Electrolysis of the complex formed in the system IBr–KBr is therefore accompanied by electrolysis of iodine bromide. According to the literature [16], during electrolysis of iodine bromide, bromine is deposited at the silver anode and iodine at the cathode.

If we assume that the same complex ($KIBr_2$) is formed in the system IBr–KBr as was obtained from a solution of KBr in fused IBr, then we must conclude that the increase in iodine content of the catholyte substantially represents the difference between the amounts of iodine transferred to the catholyte during electrolysis of IBr and to the anolyte during electrolysis of the $KIBr_2$ complex.

If we also apply the considerations which were expounded in the communication dealing with the system ICl–KCl [10], then we may conclude that in systems of the composition which we have investigated the electrolysis of each mole of $KIBr_2$ is accompanied by electrolysis of approximately 2 moles iodine bromide.

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[*] An explanation of this phenomenon is given in a previous communication [10].

[**] The same procedure was followed in the investigation of the system IBr–$AlBr_3$.

2. System IBr—$AlBr_3$. Thermal Analysis.

The same difficulties were encountered in determination of the crystallization temperatures of this system as in the investigation of the system ICl—$AlCl_3$. Visual observations of the crystallization temperatures of solutions of $AlBr_3$ in iodine bromide permitted the determination of temperature arrests only in the concentration region up to 12 mole % $AlBr_3$. Further rise in the $AlBr_3$ concentration resulted in strongly undercooled solutions which at room temperature took the form of a highly mobile liquid; these solutions did not crystallize even when cooled in solid carbon dioxide; in these conditions they formed a viscous, ropy liquid. These phenomena were observed in the concentration range of 12 to 40 mole % $AlBr_3$. Melts containing over 40 mole % $AlBr_3$ crystallized on cooling, but with very small thermal effects which could not easily be detected with the help of a thermometer.

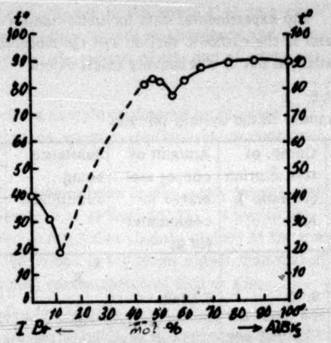
TABLE 2

Thermal Analysis of the System IBr—$AlBr_3$

Mole % $AlBr_3$	Temp. arrests	Mole % $AlBr_3$	Temp. arrests
IBr	40.0°	60.0	83.0
8.0	31.5	66.1	89.0
12.3	18.0	75.6	89.0
44.6	82.0	86.9	90.0
51.7	85.0	100.0	90.0
52.7	83.0		
53.6	82.0		
54.6	78.0		

These difficulties could only be overcome by utilizing the autorecording apparatus of N.S. Kurnakov. With the help of an automatic photorecorder and a simple, differential thermocouple it was possible to establish the melting and crystallization points for the concentration range of 44 to 87 mole % $AlBr_3$. The results of thermal analysis obtained visually and with the photorecorder are presented in Table 2 and in the diagram.

The region of strong undercooling is indicated in the diagram by the broken line; this starts near the first eutectic (about 12 mole % $AlBr_3$, m.p. 18°). The second eutectic (m.p. 78°) contains 54.6 mole % $AlBr_3$, while the distectic with m.p. 85° corresponds to a content of 51 mole % $AlBr_3$, which confirms the formation of a compound of equimolar composition.



Melting diagram of the system IBr—$AlBr_3$.

Electrolysis and Ion Transfer in the System IBr—$AlBr_3$

Electrolysis of the system IBr—$AlBr_3$ was performed on a solution containing very nearly 30 mole % $AlBr_3$. Experiments were carried out in a small U-shaped cell with platinum electrodes. Duration of experiments 3-6 hours; current strength 14 to 2 mA. For maintenance of the melt in the liquid state the cell was placed in a thermostat at 40-45°. On the surfaces of the cathode were deposited dark-grey crystalline films resembling iodine; the anode was covered with a brown precipitate. Qualitative tests showed that the cathodic deposit consisted of iodine; the anodic deposit, after washing with ether, was found to contain aluminum and bromine. Consequently, the electrolysis of the system IBr—$AlBr_3$ gave results completely analogous with those observed in the electrolysis of the system ICl—$AlCl_3$.

Ion transfer experiments were performed with solutions containing 25-27 mole % $AlBr_3$. Duration of experiments 40-50 hours with a current strength of nearly 2 mA.

Investigation of this sytem met with the same difficulties as in the system ICl—$AlCl_3$: fairly high melting point (around 85°) of the system IBr—$AlBr_3$ at concentrations close to the equivalent composition, high viscosity of the undercooled solutions, excess of iodine bromide in solution, low stability of the IBr · $AlBr_3$ complex, etc. The results of these experiments (Table 3) showed that iodine is transferred to the cathode and aluminum and bromine (in the form of a complex anion) to the anode.

Evaluation of Results. The results of investigation of the systems ICl—KCl and IBr—KBr demonstrate their great similarity; in both of these systems and in nitrobenzene solutions a complex of the same type is formed: $K[IX_2]$ where X = Cl or Br. The above-noted difference between the electric conductivities of these systems is probably due to the differing stabilities of the $KICl_2$ and $KIBr_2$ complexes.

TABLE 3

Ion Transfer in the System $IBr-AlBr_3$

No. of Expt.	Mole % $AlBr_3$	Amount of copper separated in the coulometer (in g)	Substance determined	Solution after electrolysis				Transfer number		Number of transferred milligram-atoms
				Cathodic portion		Anodic portion		Cathodic portion	Anodic portion	
				Calculated (g)	Found (g)	Calculated (g)	Found (g)			
1	25,40	0,0800	Al	0.6192	0,6113	0.3243	0.3321	0.12	0.12	0.29
			I	8.5765	8.7192	4.4924	4.3476	0,45	0.45	1.12
			Br	10.9066	10.6701	5.7129	5.9510	1.17	1.18	2.28
2	37.10	0.0972	Al	0.6839	0,6742	0.6172	0.6270	0.12	0.12	0.36
			I	5.4453	5,5732	4.9167	4.7880	0.33	0.33	1.01
			Br	9.5083	9,2188	8,5800	8.8631	1.18	1.16	3.54

The fact that the order of magnitude of electric conductivity of a nitrobenzene solution of $ICl-KCl$ is different from that of a nitrobenzene solution of $IBr-KBr$ (the first system has a rather better conductivity) might be accounted for by the $KIBr_2$ complex in nitrobenzene solution being more associated than the $KICl_2$.

An equimolar complex, $IBr \cdot AlBr_3$, appears to exist in the system $IBr-AlBr_3$, judging by the data of thermal analysis and by viscosity measurements, whereas a complex of the composition $2ICl \cdot AlCl_3$ is found in the system $ICl \cdot AlCl_3$ judging by the data of thermal analysis. The difference may be due to the circumstance that iodine chloride in the fused state (and also in some nonaqueous solvents) is associated into dimeric molecules which are apparently in equilibrium with the monomer. The dimer dissociates into ions according to the scheme $I_2Cl_2 \rightleftharpoons I^+ + ICl_2^-$. We may, consequently, represent the reaction of complex formation with iodine chloride in the form: $I[ICl_2] + AlCl_3 \rightleftharpoons I^+[AlCl_3 \cdot ICl_2]^-$.

As already noted, complexes of such a composition may undergo stepwise dissociation: $2IX \cdot AlX_3 \rightleftharpoons IX \cdot AlC_3 + IX$. Independently of this difference in composition, the complexes identified by physicochemical analysis of the systems $ICl-AlCl_3$ and $IBr-AlBr_3$ are identical in electrochemical behavior, as shown by measurements of electric conductivity, by electrolysis and by ion transfer data: the cation of these complexes is iodine, while aluminum and chlorine (or bromine) enter into the composition of the complex anion.

SUMMARY

1. The processes of electrolysis and ion transfer in the systems $IBr-KBr$ and $IBr-AlBr_3$ have been studied. It is shown that in respect of the character of the complexes formed in these systems, the latter are very similar to the analogous systems comprising iodine chloride and potassium and aluminium chlorides.

2. A complex of equimolar composition was identified in the system $IBr-AlBr_3$ by the method of thermal analysis.

3. The properties of the systems $ICl-KCl$ and $IBr-KBr$, $ICl-AlCl_3$ and $IBr-AlBr_3$ are compared.

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THE STRUCTURES AND NATURE OF THE COMPLEX COMPOUNDS FORMED BY REACTION OF IODINE HALIDES WITH POTASSIUM OR ALUMINUM HALIDES*

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In previous communications devoted to the physicochemical study of the systems IX–KX and IX–AlX_3 (X = Cl or Br) and of the same systems in nitrobenzene solutions [1-6], experimental data were put forward which demonstrated the formation of complex compounds of the type of KX · IX, AlX_3 · IX and AlX_3 · 2IX. In the same researches Ya. A. Fialkov, K. Ya. Kaganskaya and O.I. Shor discussed the nature and structure of complex compounds of this type.

In the present communication we give more detailed consideration to this problem, mainly on the basis of results of a study of electrolysis and ion transfer.

As a preliminary we must generalize on certain experimental data bearing on the electrochemical properties of the systems in question and of the complex compounds formed.

a) We must point out in the first place that compounds formed in systems consisting of iodine halides and potassium or aluminium halides are fairly good electrolytes: the specific electric conductivity of these systems is of the order of 10^{-3} to 10^{-2} $ohm^{-1}cm^{-1}$.

b) As was shown by a study of nitrobenzene solutions of these systems by the cryoscopic method, complexes of iodine halides with potassium or aluminum halides are capable of association in these solutions.

c) Data for electrolysis* of systems consisting of potassium halides and iodine halides point to the conclusion that the products of electrolysis at the cathode are potassium and a small amount of iodine formed by electrolysis of the excess of iodine halides, while at the anode there is chlorine (or bromine). In the case, however, of electrolysis of nitrobenzene solutions of these systems, potassium accumulates in the catholyte and iodine and chlorine (or bromine) in the anolyte.

d) In the electrolysis of systems containing iodine halides and aluminum halides, iodine goes into the catholyte and aluminum and chlorine (or bromine) into the anolyte in the form of the complex anion. On electrolysis of the nitrobenzene solutions of iodine halides and aluminum halides, however, the anolyte acquires an increased content of aluminum as well as of both halogens.

Comparison and elucidation of the quantitative results on ion transfer in the investigated systems are facilitated by the tables below in which the numbers of ions transferred in each experiment are expressed in g-atoms per g-atom potassium (in systems containing potassium halides) and per g-atom of aluminum (in systems containing aluminum halides) (Tables 1 and 2).

Before proceeding to consider these quantitative data, attention must be drawn to the difficulties associated with a study of these systems by the ion transfer method. Chief among these difficulties is the electrolysis – side by side with the electrolysis of the complex molecules formed in these systems – of the excess of the iodine halides***; this seriously complicates the interpretation of the quantitative results, since in the chemical analysis of the catholyte and anolyte – after electrolysis – we naturally find only the difference in the amount of iodine or other ions if they are simultaneously transferred to the catholyte and anolyte. Moreover, it was necessary to take into account the side reactions which were observed during the electrolysis of nitrobenzene solutions of the systems IX–KX and IX–AlX_3 and the resultant difference in behavior of iodine in systems containing a solvent and those not containing one.

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* Communication XI in the series on physicochemical investigation of systems containing iodine halides and halides of other elements.

** Reference is here made also to results of a study of ion transfer in these and the following systems.

*** For investigation of the binary systems it was necessary to use exess of iodine chloride or iodine bromide consequent upon: 1) the relatively low solubility of potassium halides in fused ICl or IBr; 2) the high melting point of the systems IX–AlX_3 when the content of $AlCl_3$ or $AlBr_3$ was close to 50 mole % or higher.

TABLE 1

Relative Numbers of Ions (in g-atoms) Transferred in Experiments with the Systems Iodine Halides-Potassium Halides

Ions	System ICl–KCl [5]				System IBr–KBr [6]				System IBr–$C_6H_5NO_2$ [4]			
	Experiment 1		Experiment 2		Experiment 1		Experiment 2		Experiment 1		Experiment 2	
	Catholyte	Anolyte	Catholyte	Anolyte	Catholyte	Anolyte	Catholyte	Anolyte	Catholyte	Anolyte	Catholyte	Anolyte
K	1	–	1	–	1	–	1	–	1	–	1	–
I	0.6	–	0.8	–	0.4	–	0.4	–	–	1.2	–	1.4
Cl or Br.	–	3.3	–	2.8	–	3.5	–	3.5	–	2.2	–	2.1

TABLE 2

Relative Numbers of Ions (in g-atoms) Transferred in Experiments with the Systems Iodine Halides-Aluminum Halides

Ions	System ICl–$AlCl_3$ [5]				System IBr–$AlBr_3$ [6]				System IBr–$AlBr_3$–$C_6H_5NO_2$ [4]							
	Experiment 1		Experiment 2		Experiment 1		Experiment 2		Experiment 1		Experiment 2		Experiment 1		Experiment 2	
	catholyte	anolyte	catholyte	anolyte	catholyte	anolyte	catholyte	anolyte	catholyte	anolyte	catholyte	anolyte	catholyte	anolyte	catholyte	anolyte
Al	–	1	–	1	–	1	–	1	–	1	–	1	–	1	–	1
I	1.4	–	2.6	–	3.9	–	2.8	–	–	5.2	–	8.4	–	6.3	–	6.2
Cl or Br	–	6.6	–	8.2	–	10.3	–	9.7	–	13.3	–	16.4	–	13.3	–	13.2

1. Systems of Iodine Halides-Potassium Halides

Experimental results on ion transfer in systems containing iodine halides and potassium halides (Table 1) permit the following conclusions to be drawn:

a) In iodine halide-potassium halide systems the iodine content increases in the catholyte, although to a relatively slight extent (less than 1 g-atom per g-atom of potassium transferred during the experiment), and correspondingly decreases in the anolyte. In nitrobenzene solution, however, the opposite was the case – the iodine content increased in the anodic portion of the solution.

b) On comparing the number of equivalents (or g-atoms) of chlorine or bromine required for 1 equivalent of potassium, we can infer that in nitrobenzene solutions the composition of the complex compound is evidently simpler because in the solvent-containing system less bromine is required per equivalent of potassium (from 2.1 to 2.2 equivalents) than in a solvent-free system where for each equivalent of potassium transferred to the catholyte we find 3.5 equivalents of bromine transferred to the anolyte. A similar conclusion can be reached by comparing the transfer numbers for potassium and bromine ions as determined from direct analytical data (Table 3).

TABLE 3

Transfer Numbers of Ions in the Systems Potassium Halides-Iodine Halides*

Ions	System ICl–KCl [5]		System IBr–KBr [6]		System IBr–KBr–$C_6H_5NO_2$ [4]	
	Experiment 1	Experiment 2	Experiment 1	Experiment 2	Experiment 1	Experiment 2
K	0.29	0.31	0.43	0.42	0.59	0.51
I	0.19	0.25	0.17	0.18	0.69	0.69
Cl or Br	1.00	0.91	1.50	1.47	1.31	1.04

The fact that in experiments with the systems ICl–KCl and IBr–KBr the chlorine transfer number is close to unity, while for bromine it is even higher than unity, suggests that bromine or chlorine are transferred to the anolyte in the form of a complex ion whose composition in the systems IX–KX is evidently more intricate than in the systems IX–KX–nitrobenzene.

c) The ratio of the amounts of iodine and bromine transferred to the anolyte in one and the same experiment in a nitrobenzene solution of IBr–KBr fluctuates between 1:1.5 and 1:1.8. These data agree in part with those of experiment 3 for the system ICl–KCl-nitrobenzene [3], where the ratio of iodine and chlorine transferred to the anolyte was 1:2.3. On this basis we may suggest that nitrobenzene solutions of the system IX–KX contain a complex anion with the composition IX_2^-, i.e. ICl_2^- and IBr_2^-.

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* Tables 3 and 4 present the mean values of transfer numbers calculated on the basis of analyses of the cathodic and anodic liquids.

The results of our investigation are consequently in full accord with the literature data and indicate that the complexes formed in the systems IX–KX contain potassium as cation (in presence of nitrobenzene it is possibly solvated) and iodine and chlorine or iodine and bromine in the anion.

A more detailed characterization of the investigated systems on the basis of results of a study of ion transfer necessitates knowledge of the ionic mobility or exact values of the transfer numbers. The mobility of the ions present in our investigated systems has not been studied. Greenwood and Emeleus [7], utilized the data of Fialkov and Kaganskaya [3], according to which the transfer number of ICl_2^- in the system ICl–KCl-nitrobenzene can be assumed to be equal to 0.504* (which is very close to the transfer number of Cl^- ions in aqueous solutions). They calculated the mobility of ICl_2^- ions from the magnitude of the mobility of Cl^- in water and from the ratio of the viscosities of water and nitrobenzene. The mobility of potassium ions might also be calculated by this method, but such calculations of ionic mobilities are purely arbitrary.

Concerning the transfer numbers set out in Tables 3 and 4, they fail to give full expression to the structure of the complexes formed in these systems for the following reasons:

a) In the course of ion transfer experiments not only is the complex electrolyzed but also the excess of iodine chloride or bromide present in the investigated systems,

b) The behavior of iodine in the binary systems is different from that in their nitrobenzene solutions; in the latter the iodine liberated at the cathode by discharge of I^+ ions is subsequently transferred to the anolyte due to side reactions [8].

TABLE 4

Ion Transfer Numbers in Systems of Aluminum Halides-Iodine Halides

Ions	System $ICl-AlCl_3$ [5]		System $IBr-AlBr_3$ [6]		System $IBr-AlBr_3-C_6H_5NO_2$ [4]			
	Experiment 1	Experiment 2	Experiment 1	Experiment 2	Experiment 1	Experiment 2	Experiment 3	Expt 4
Al	0.13	0.13	0.12	0.12	0.11	0.11	0.10	0.12
I	0.23	0.33	0.45	0.33	0.59	0.87	0.65	0.69
Cl or Br. .	1.03	1.08	1.18	1.17	1.48	1.73	1.38	1.60

Nevertheless, on the basis of our experimental data it is possible to establish the composition of the complex and to give an approximate quantitative characterization of the reactions taking place during electrolysis of the investigated systems if we compare the transfer numbers or numbers of equivalents (or g-atoms) of ions which are transferred in the course of the electrolysis. The lack of data for mobility of ions compels us to perform the evaluation on the basis of whether or not the mobilities of the ions in the investigated systems are equal.

As we know the mobilities of K^+, Cl^-, Br^- and I^- ions in aqueous solutions are very similar; it is permissible to assume that they will not differ appreciably also in the systems under investigation. Here we may also remark that Greenwood and Emeleus [7] assume that the mobilities of I^+ and ICl_2^- ions are the same.

Let us apply such considerations to the system ICl–KCl as an example. In order to obtain an approximate idea of the state of this sytem in the course of electrolysis, we must start from the assumption that ion transfer in that system is the result of electrolysis of the complex compound formed in the system and of electrolysis of the excess of iodine chloride; furthermore, we shall assume that the mobilities of the ions in these systems are identical.

If we assume on the basis of preparative studies that the composition of this complex compound is represented by the formula $KICl_2$, then the electrolysis of one mole of such a compound causes one equivalent of potassium to go into the catholyte and one equivalent of iodine and two equivalents of chlorine to go into the anolyte. Let us assume that at the same time electrolysis takes place of x moles iodine chloride, so that this would entail the transfer of x equivalents of iodine to the catholyte and of x equivalents of chlorine to the anolyte.

It follows that in the electrolysis of the system ICl–KCl containing an excess of x moles iodine chloride over the equimolar ratio ICl:KCl, transfer will take place to the catholyte of one equivalent of potassium and of (x−1) equivalents of iodine; at the same time (2 + x) equivalents of chlorine will go to the anolyte.

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* In this work Fialkov and Kaganskaya determined the transfer number only for K^+ ions. It was found to be 0.496, i.e. very close to the transfer number of K^+, in aqueous solutions of KCl (0.498). Greenwood and Emeleus calculated the transfer number of ICl_2^- on the assumption that the complex is represented by the formula $K[ICl_2]$.

We are now in a position to calculate the ratios of equivalents of potassium, iodine and chlorine for various values of x.

According to Cornog and Bauer [9], in the system ICl−KCl at temperatures below 45° the formation is possible of an unstable compound KI_2Cl_3 (or KCl · 2ICl). Assuming that a complex of this composition is formed in the KCl−ICl melt, investigated by us, and that the electrolysis of one mole KI_2Cl_3 is accompanied by electrolysis of x moles ICl, we then obtain the following values: transfer takes place to the catholyte of one equivalent of potassium and (x−2) equivalents of iodine, and to the anolyte of (x + 3) equivalents of chlorine.

A comparison of the experimentally found ratios of equivalents of potassium, iodine and chlorine with those calculated as above, confirms that in the system KCl−ICl which we have investigated, the complex $KICl_2$ is subjected to electrolysis. Thus, for example, from the results of the first experiment with the system KCl−ICl (Table 1), the following ratio of equivalents of potassium, iodine (transferred to the catholyte) and chlorine (transferred to the anolyte) is obtained: K:I:Cl = 1:0.6:3.3. These values for iodine and chlorine are higher than those calculated on the assumption that x = 1 (K:I:Cl = 1:0:3) and lower than those on the basis of x = 2 (1:1:4). But if we assume that the mobilities of the ions in the investigated systems are not equal (which is more probable) and that the mobility of the K^+ ion is manifestly greater than that of the ICl_2^- ions, while the mobility of I^+ is lower than that of Cl^-, then a calculation similar to the above one for the system $K[ICl_2] + xICl$ gives the ratio K:I:Cl = 1:0:<3 (for x = 1) or 1:<1:<4 (for x = 2).

From the above considerations we may conclude that the electrolysis of 1 mole $KICl_2$ is accompanied by electrolysis of 2 moles iodine chloride, and this would explain the increased transfer of iodine (I^+) to the cathode in comparison with its transfer to the anode in the form of ICl_2^- complex anion. We must remember that in this experiment electrolysis was performed on a solution of 5.5 mole % KCl in fused iodine chloride, i.e., a solution containing a considerable excess of iodine chloride.

This conclusion is confirmed by the results of the second experiment with a melt likewise containing 5.5 mole % KCl.

Thus, the ratios based on the hypothesis that the unstable complex KI_2Cl_3 exists in the KCl−ICl melt are altogether inconsistent with the experimental data. For example, if the hypothesis were correct, there should have been observed a transfer of iodine to the anolyte, whereas in our experiments we observed a transfer of iodine to the catholyte, even though in very small quantity. In the event of formation of KI_2Cl_3, a transfer of iodine to the catholyte would only have been observed after supplementary electrolysis of 3 moles of iodine chloride (x = 3), but in that case 6 equivalents of chlorine would have gone to the anolyte and such a transfer was not observed by us.

Turning now to the quantitative interpretation of the experimental results for ion transfer in the system IBr−KBr, we apply the same calculations as for the system ICl−KCl.

Comparison of the experimentally determined ratios of equivalents of potassium, iodine and bromine with the calculated values permits the conclusion that in the system IBr−KBr the complex $KIBr_2$ undergoes electrolysis.

The ratio of the equivalents of potassium, iodine and bromine, from the data of both experiments (K:I:Br = 1:0.4:3.5),• is close to the ratios calculated for x = 2 and on condition that the mobilities of ions of K^+ and IBr_2^- (etc.) are not equal (K:I:Br = 1:<1:<4).••

From these data we draw a conclusion similar to that for the system ICl−KCl, namely, that during electrolysis of one mole of $KIBr_2$ electrolysis takes place of 2 moles of iodine bromide.

In the nitrobenzene solution of the system IBr−KBr the ratios of the number of equivalents of ions of potassium and halogens transferred during electrolysis were much simpler (K:I:Br = 1:1.2:2.2 or 1:1.4:2.1) than in the binary systems IX−KX (Table 1). Moreover, in the electrolysis of nitrobenzene solutions of these systems, even when they contained an excess of iodine halide over that corresponding to an equimolar ratio of iodine halide to potassium halide, transfer of both halogens to the anode was observed.

• The concentration in the first case was 8.4 and in the second case 9.7 mole % KBr in IBr melt.

•• Reference is to transfer of K^+ and I^+ to the catholyte and of Br_2^- ions to the anolyte (Table 1).

The explanation of the last observation is that the molecular iodine formed at the cathode by discharge of I^+ ions undergoes cathodic reduction ($I_2 + 2\underline{e} \rightarrow 2I^-$) and is transferred to the anode; another possibility is the formation of complexes with the solvent, likewise leading to transformation into I^- ions which go to the anode. Transfer of iodine and chlorine to the anode was observed by Bruner and Galecki [10], also by Fialkov and Kaganskaya [2]; according to the last authors for each $\underline{F}$ there was transferred to the anolyte a little less than one equivalent of iodine and about 1.5 equivalents of chlorine.*

On the basis of the above data we may conclude that the complex $K[IBr_2]$ is present in the nitrobenzene solutions of IBr–KBr that we investigated (molar ratio IBr : KBr = 1 : 0.22-0.23) and that the electrolysis of one mole of this complex is accompanied by electrolysis of about 0.5 mole of excess iodine bromide.

In conclusion we may say that, making allowance for the complexity of the systems ICl–KCl and IBr–KBr, as well as for the experimental difficulties, the agreement between our experimental and calculated data is sufficiently good and permits us to claim that compounds whose most probable composition is $KICl_2$ and $KIBr_2$ are formed in the systems IX–KX and IX–KX–nitrobenzene.

2. Systems of Iodine Halides-Aluminum Halides

A characteristic feature of the behavior of ions in the systems $IX-AlX_3$ during their electrolysis is transfer of aluminum and chlorine (or bromine) to the anode and of iodine to the cathode (Table 2). From this it follows that iodine is present as cation in the complex compound formed in systems containing iodine halides and aluminum halides, while the anion consists of aluminum and chlorine or aluminum and bromine and is probably solvated by iodine chloride or bromide as evidenced by the large number of g-atoms of chlorine and bromine transferred to the anolyte. The iodine is transferred to the cathodic portion and chlorine (or bromine) to the anodic portion partly as a result of electrolysis of excess iodine halides.

The melting curve of the system $ICl-AlCl_3$ indicates the formation of an unstable compound with the composition $AlCl_3 \cdot 2ICl$ [5]. Taking into account the fact that in ion transfer experiments each g-atom aluminum was accompanied to the anolyte by 7-8 g-atoms of chlorine, we may assume that we are dealing with the complex $I[AlCl_4]$ whose anion is solvated by iodine chloride.

Formation of such solvated complexes is favored by the iodine chloride molecules being associated in the liquid state, in the simplest case as $[I_2Cl_2]$. According to Sandonini and Berghello [11] the latter molecules dissociate into I^+ and ICl_2^-.

Regarding the system $IBr-AlBr_3$, a study of the viscosity [1] and of data for thermal analysis [6] supports the formation of the complex $I[AlBr_4]$.

The results of ion transfer experiments (Table 2) and in particular the high transfer number of bromine (>1) in this system (Table 4), indicate that this complex is likewise susceptible to solvation by iodine bromide.

From the ion transfer data (Tables 2 and 4) the composition of the complex ions in the systems $ICl-AlCl_3$ and $IBr-AlBr_3$ can be established by a procedure similar to that applied for the systems ICl–KCl and IBr–KBr.

Of the possible variants we shall consider the following simplest cases.

1. The complex $I[AlX_4]$ undergoes electrolysis to the accompaniment of electrolysis of $\underline{x}$ moles iodine chloride or bromide. Consequently, $\underline{x} + 1$ g-atoms iodine will go to the catholyte and $\underline{x} + 4$ g-atoms chlorine or bromine**will go to the anolyte with each g-atom of aluminum.

But since the mobility of $[AlX_4]^-$ ions is evidently lower than the mobility of ions of I^+ and Cl^- (or Br^-), then for each g-atom of aluminum transferred to the anolyte in the form of complex anion, transfer must take place to the catholyte of rather more than $\underline{x} + 1$ g-atoms of iodine, and to the anolyte of slightly more than $\underline{x} + 4$ g-atoms chlorine or bromine.

2. Electrolysis is undergone by the complex $I[AlX_4]$, solvated with $\underline{y}$ moles of IX. At the same time $\underline{x}$ moles of iodine halide (ICl or IBr) are electrolyzed.

If we assume that $\underline{y} = 1$, i.e., that electrolysis is undergone by the complex $I[AlX_4 \cdot IX]$ or $I[X_3AlIX_2]$. content should not change appreciably either in the anolyte or in the catholyte. But if $\underline{y}$ is equal to 2 or more, than not only will the content of aluminum and chlorine in the anolyte increase but also the content of iodine. Each g-atom aluminum requires $(\underline{y}-1)$ g-atoms iodine and $(\underline{y}+4)$ g-atoms chlorine (or bromine).

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* It must be remembered that the nitrobenzene solution contain dimeric molecules: $I_2Cl_2 \quad I^+ + ICl_2^-$ [2].

** In this case it more convenient to base the calculation not on g-equivalents but on g-atoms because the composition of the simplest complex, $I[AlX_4]$, solvated with $\underline{y}$ moles of IX. At the same time $\underline{x}$ moles of iodine halide (ICl or IBr) are electrolyzed.

But if electrolysis simultaneously takes place also of $\underline{x}$ moles IX, then $(\underline{x}-\underline{y}+1)$ g-atoms iodine will go to the catholyte, and 1 g-atom aluminum and $(\underline{x}+\underline{y}+4)$ g-atoms chlorine (or bromine) to the anolyte.

Let us compare the so-calculated values with the experimental ones set out in Table 2 for the system $ICl-AlCl_3$. This comparison shows that the values for the first experiment (Al: I: Cl = 1: 1.4: 6.6) are very close to those calculated on the assumption that $\underline{y} = 1$ and $\underline{x} = 1$ (Al: I: Cl = 1: 1: 6).* This corresponds to simultaneous electrolysis of the complex $I[AlCl_4 \cdot ICl]$ and 1 mole iodine chloride.

The ratios obtained from the data of experiment 2 (Al: I: Cl = 1: 2.6: 8.2) are close to those calculated on the assumption that $\underline{y} = 1$ and $\underline{x} = 3$ (Al: I: Cl = 1: 3: 8), which corresponds to the electrolysis of $I[AlCl_4 \cdot ICl]$ and approximately 3 moles iodine chloride. It must be noted that a larger excess of iodine chloride was taken in this experiment than in experiment 1 (in experiment 1 the $AlCl_3$ concentration was 28.8 mole % and in experiment 2 it was 20.6 mole %).

As for the hypothesis that the nonsolvated complex is electrolyzed, the ratios of g-atoms of iodine, aluminum and chlorine transferred in course of electrolysis on this basis are entirely at variance with the experimental data.

Comparison of the experimentally found ratios of amounts of iodine, aluminum and bromine transferred to the catholyte and anolyte during investigation of the system $IBr-AlBr_3$ with the calculated values permits us to draw the conclusion that the complex $I[AlBr_4]$ is solvated by two moles of iodine bromide.

Thus, for instance, the data of experiment 1 for the system $IBr-AlBr_3$ (Al: I: Br = 1: 3.9: 10.3) are close to the values calculated on the assumption that $\underline{y} = 2$ and $\underline{x} = 4$ (Al: I: Br = 1:>3:>10). The results of experiment 2 (Al: I: Br = 1: 2.8: 9.7) are close to the g-atom ratios when $\underline{y} = 2$ and $\underline{x} = 3$. Consequently, electrolysis of the complex $I[AlBr_4 \cdot 2IBr]$ proceeds to the accompaniment of electrolysis of 3-4 moles (depending on the concentration of the starting solution) of iodine bromide. It should be noted that in experiment 1 the concentration of aluminum bromide was 25.4 mole %, while in experiment 2 it was 37.1 mole %.

In attempting a similar characterization of the system $IBr-AlBr_3$–nitrobenzene we come up against even greater difficulties. First, as already noted in the electrolysis of this sytem, the anodic portion receives an increased amount of not only aluminum but also of both halogens. Second, the number of equivalents of bromine transferred to the anolyte reaches quite a high figure.

The fact is that in the system $IBr-AlBr_3$–nitrobenzene the secondary electrolytic processes are more diverse and more complex than in the analogous system containing potassium bromide: The primary transfer of iodine to the catholyte proceeds not only via electrolysis of the excess iodine bromide, but also via electrolysis of the complex $AlBr_3 \cdot \underline{n}IBr$. The iodine discharged at the cathode subsequently begins to move to the anode.

Moreover, this complex is considerably less stable than $KIBr_2$, and in solution it probably exists in equilibrium with its constituents – IBr and $AlBr_3$.

As we know from the literature [12, 13], a solution of aluminum bromide in nitrobenzene is a conductor. The investigations of Sheka and Pechenaya [14] have established that the cations in such a system are aluminum ions solvated with nitrobenzene. The anions in dilute solutions are predominantly simple bromine ions, but in more concentrated solutions the bromine ions exist side by side with complex anions: $AlBr_4^-$, $Al_2Br_7^-$ etc., which are solvated by nitrobenzene.

These simultaneously occurring processes complicate the calculations along the lines of the schemes exemplified above. We are, therefore, compelled to limit ourselves to stating that the complex formed in nitrobenzene solution has the same nature and the same approximate composition as in the solvent-free system, i.e., it consists of $I[AlBr_4]$ solvated with iodine bromide.

The structure of complex compounds of $AlCl_3$ or $AlBr_3$ with iodine halides, of the type of $AlX_3 \cdot \underline{n}IX$, may be represented by the following schemes:

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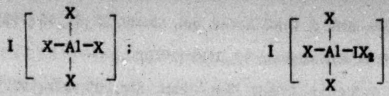
* On the assumption that the ionic mobilities are not equal and that the mobility of aluminum containing complex anions must be lower than that of halogens, the ratio of the transferred amounts is Al: I: Cl = 1:>1:>6.



$$I\left[\begin{matrix} & X & \\ & | & \\ X- & Al & -X \\ & | & \\ & X & \end{matrix}\right]; \qquad I\left[\begin{matrix} & X & \\ & | & \\ X- & Al & -IX_2 \\ & | & \\ & X & \end{matrix}\right]$$

etc.

With maintenance of a coordination number of 4 for aluminum the molecules of AlX_3 can combine with a maximum of 5 molecules of iodine halide with formation of the complex $I[Al(IX_2)_4]$.

In a study of the system $ICl-SbCl_3$, Ya. A. Fialkov and I.L. Abarbachuk established the existence of the analogous complex compounds $SbCl_3 \cdot 4ICl$ and $SbCl_3 \cdot 5ICl$ [15], containing antimony in the complex ion; the cation is iodine. Their structure is evidently the same as that of complex compounds of aluminium halides with iodine halides.

The complex compounds $AlX_3 \cdot \underline{n}IX$ have low stability and readily undergo dissociation. Rise of temperature accelerates dissociation and leads to cleavage of the iodine halides which had solvated the complex. This is demonstrated by the detection of only a compound with the composition $IBr \cdot AlBr_3$ on the melting curve of the system $IBr-AlBr_3$ at 100° [6], as well as in a study of the viscosity of this sytem [1].

The results of the investigations show that not only highly polar alkali metal halides but also the nonpolar aluminum halides combine with iodine halides to form complexes of the type of binary halides. These complexes are differentiated in structure: The nonpolar aluminum halides combine with iodine chloride or bromide and enter into the composition of complex anions; but the highly polar potassium halides combine with iodine halides in such a manner as to form a complex anion at the expense of their halogen ions, Cl^- and Br^-, and of the iodine halides.

Although compounds of the type of $KCl \cdot ICl$ or $K[ICl_2]$ can be classed as double halides, they are nevertheless closely related to complexes of the polyhalide type and constitute, so to speak, intermediates between the polyhalides — products of addition of molecules of halides to halide anions — and complexes of the double-salt type.

Complex compounds of the type of $I[AlX_4]$ or $I[AlX_4 \cdot \underline{n}IX]$, also similar compounds of $SbCl_3$ with ICl, are the first representatives of a new series of double halides whose cation is iodine.

SUMMARY

1. An evaluation is made of the results of a study of ion transfer in the systems $IX-KX$ and $IX-AlX_3$ ($\underline{X}$ being Cl or Br) and of their nitrobenzene solutions.

2. A quantitative characterization is performed of the processes taking place during electrolysis of these systems.

3. Consideration is given to the problem of the composition, structure and nature of the complex compounds formed in these systems in the form of double halides of the general formula $K[IX_2]$ and $I[AlX_4 \cdot \underline{n}IX]$ or $I[AlX_{4-n}(IX_2)_n]$.

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AN IRREVERSIBLE-RECIPROCAL SYSTEM OF THE SINGULAR TYPE WITH LAYER FORMATION FROM THE SULFATES AND CHLORIDES OF LITHIUM AND SILVER

D. S. Lesnykh and A. G. Bergman

Analysis of the ternary reciprocal systems of chlorides and sulfates which have been investigated by us and by other authors shows that all the systems with participation of salts of lithium and salts of alkali metals and alkaline earth metals (separately) belong to the type of systems with unlimited reciprocal solubility of the components in the fused state. But in systems with participation of salts of lithium and thallium, lithium and lead, and lithium and cadmium, there is limited reciprocal solubility in melts of the components of stable pairs. On the other hand, the components of stable pairs of chloride-sulfate systems with participation of salts of silver and thallium [1] and silver and cadmium [2] only have a tendency to form layers, whereas in the system constituted by the salts of silver and sodium [3] the components of the stable pair exhibit limited reciprocal solubility in the fused state.

TABLE 1

Binary Systems (Fig. 1).

Systems	Characteristic points of curve	Data of other authors		Our data	
		%*	M.p.	%	M.p.
$LiCl \rightarrow AgCl$	Continuous series of solid solutions without minimum and maximum	[5]		—	—
	Homeomorphic transformation of LiCl	—	—	—	560
$Ag_2Cl_2 \rightarrow Ag_2SO_4$	Eutectic	47	304 [1]	—	—
	Polymorphic transformation of Ag_2SO_4	—	412	—	—
$Ag_2SO_4 \rightarrow Li_2SO_4$	Congruent compound $3Ag_2SO_4 \cdot 2Li_2SO_4$, giving a continuous series of solid solutions with the components	40	572 [5]	—	—
	Eutectic I	—	—	25	567
	Congruent compound $Ag_2SO_4 \cdot Li_2SO_4$	—	—	50	575
	Eutectic II	—	—	68.5	556
$Li_2Cl_2 \rightarrow Li_2SO_4$	Eutectic	53.5	478 [6]	53	478
	Polymorphic transformation of Li_2SO_4	—	572	—	572
	Homeomorphic transformation of LiCl	—	—	—	564

These facts justify the assumption that layer formation in melts in the majority of cases is due to the presence in the system of ions with a different structure of the outer electron shells (inert-gas type on the one hand, and containing 18 or 18 + 2 electrons on the other hand), possessing a different polarization character and forming salts of a stable pair with sharply divergent physicochemical properties. An exception is provided by the system of chlorides and sulfates of lithium and zinc, whose components exhibit unlimited solubility in the liquid state and tend strongly to form complexes.

For the purpose of confirming the above hypothesis we have studied the ternary reciprocal system of the chlorides and sulfates of lithium and silver in melts by the visual-polythermic method. Another aim of the investigation was the clarification of the influence of exchange of anions: Substitution of I' in a system with stratification of Li, Ag || Cl, I [4] and of NO_3' in a system with stratification of Li, Ag || Cl, NO_3 by the SO_4'' ion.

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* Equimolar percentages of the added component.

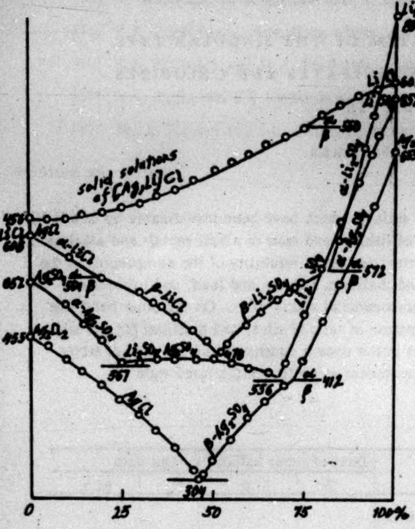

Fig. 1. Sides of the square of the reciprocal system.

Diagonal sections (Fig. 2). The thermal effect of the reaction $Li_2Cl_2 + Ag_2SO_4 \longrightarrow Ag_2Cl_2 + Li_2SO_4$ is equal to 17.8 kcal per equivalent. The stable diagonal section $Ag_2Cl_2-Li_2SO_4$ has the character of a binary system with a eutectic at 44.5° and 0.4% lithium sulfate. The components of the stable pair possess extremely limited reciprocal solubility in the fused state – the interval of stratification extends from 2 to 98.8% lithium sulfate at 818°. The melting curve is broken by a straight line parallel to the composition axes, due to a three-phase monotectic process. The curve is represented by a broken line up to 26% Li_2SO_4, consequent upon the experimental difficulty of determination of the crystallization temperatures of very fine drops of lithium sulfate.

The melting diagram of the unstable section of $Li_2Cl_2-Ag_2SO_4$ consists of six crystallization branches: α,β-continuous solid solutions [Ag, Li]Cl, β,α-sulfates of lithium, and β,α-sulfates of silver which are intersected respectively at 564° and

In the interval from 22.5% Ag_2SO_4 at 492° to 72.5% Ag_2SO_4 at 518° the melt separates into two liquid phases.

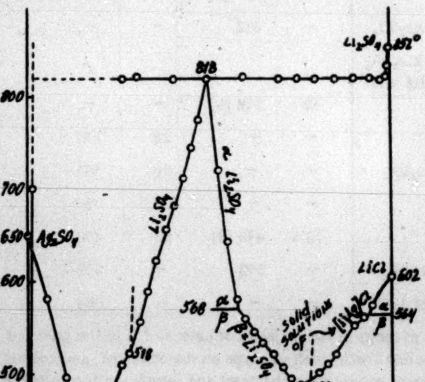

Fig. 2. Diagonal sections.

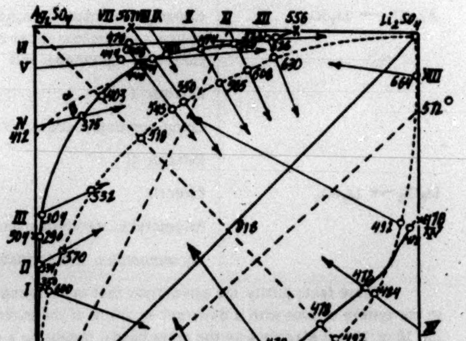
Ag2SO4
VII
IX
X
XI
XII
556
Li2SO4
VI
V
XIII
664
572°
IV
412
375
403
510
III
309
304
290
II
570
I
818
492
470
478
484
XV
664
478
492
478
487
490
482
478
445
Ag2Cl2
XIV
468
XVIII
XVII
XVI
Li2Cl2
β
α

Fig. 3. Directions of internal sections.

Reciprocal system. The surface of primary separations of crystals was investigated with the help of nineteen internal sections whose directions are shown in Fig. 3; a short characterization of each of them is given in the summary table and in Figs. 4 and 5.

TABLE 2

Summary Table of Internal Sections of the Reciprocal System

No. of section	Initial mixture of components	M.p. of starting mixture	Added component	Branches of crystallization curves and their intersections: Branch I	Intersections of I and II		Branch II	Intersections II and III		Branch III	Start of stratification		
					%*	t°		%	t°		%	t°	
I	65% Ag_2Cl_2+35% Ag_2SO_4	358	Li_2Cl_2	Ag_2Cl_2	0.5	358	Li_2SO_4				3	600	4
II	60% Ag_2Cl_2+40% Ag_2SO_4	340	Li_2SO_4	Ag_2Cl_2	0.5	334	Li_2SO_4				7.5	570	4
III	47.5% Ag_2Cl_2+52.5% Ag_2SO_4	338	Li_2SO_4	β-Ag_2SO_4	1.5	304	Li_2SO_4				15	532	4
IV	25% Ag_2Cl_2+75% Ag_2SO_4	432	Li_2SO_4	α-Ag_2SO_4	2.5	412	β-Ag_2SO_4	12.5	375	Li_2SO_4			4
V	10% Ag_2Cl_2+90% Ag_2SO_4	550	Li_2SO_4	α-Ag_2SO_4	22.5	444	Compound Ag_2SO_4·Li_2SO_4	30	444	Li_2SO_4			4
VI	5% Ag_2Cl_2+95% Ag_2SO_4	600	Li_2SO_4	α-Ag_2SO_4	25	479	Compound Ag_2SO_4·Li_2SO_4	62.5	526	Li_2SO_4			4
VII	80% Ag_2SO_4+20% Li_2SO_4	590	Li_2Cl_2	α-Ag_2SO_4	5.5	458	Compound $\underline{AB}$	9	440	Li_2SO_4	20	545	4
VIII	75% Ag_2SO_4+25% Li_2SO_4	570	Li_2Cl_2	Ag_2SO_4··Li_2SO_4	7.5	443	Li_2SO_4				18	550	4
IX	70% Ag_2SO_4+30% Li_2SO_4	570	Li_2Cl_2	Compound Ag_2SO_4··Li_2SO_4	6	456	Li_2SO_4						4
X	60% Ag_2SO_4+40% Li_2SO_4	573	Li_2Cl_2	Compound Ag_2SO_4··Li_2SO_4	5	474	Li_2SO_4				13.5	585	4
XI	50% Ag_2SO_4+50% Li_2SO_4	575	Li_2Cl_2	Compound Ag_2SO_4··Li_2SO_4	3.5	500	Li_2SO_4				10	608	5
XII	40% Ag_2SO_4+60% Li_2SO_4	567	Li_2Cl_2	Compound Ag_2SO_4·Li_2SO_4	2	522	Li_2SO_4				7	630	5
XIII	90% Li_2SO_4+10% Li_2Cl_2	664	Ag_2SO_4	α-Li_2SO_4							1	664	5
XIV	50% Li_2SO_4+50% Li_2Cl_2	492	Ag_2SO_4	Solid solutions [Ag, Li]Cl	2.5	478	β-Li_2SO_4	22.5	572	α-Li_2SO_4	5	492	5
XV	25% Li_2SO_4+75% Li_2Cl_2	554	Ag_2SO_4	Solid solutions [Ag, Li]Cl	14	478	β-Li_2SO_4				12.5	484	5
XVI	25% Ag_2Cl_2+75% Li_2Cl_2	554	Ag_2SO_4	Solid solutions [Ag, Li]Cl	16.5	478	β-Li_2SO_4	35	572	α-Li_2SO_4	12.5	487	5
XVII	50% Ag_2Cl_2+50% Li_2Cl_2	509	Ag_2SO_4	Solid solutions [Ag, Li]Cl	5	478	β-Li_2SO_4				5	478	5
XVIII	60% Ag_2Cl_2+40% Li_2Cl_2	491	Ag_2SO_4	Solid solutions [Ag, Li]Cl	2.5	478	β-Li_2SO_4				3	482	5
XIX	75% Ag_2Cl_2+25% Li_2Cl_2	468	Ag_2SO_4	Solid solutions (Ag, Li]Cl	0.5	465	β-Li_2SO_4				1	490	5

* Percent of additive.

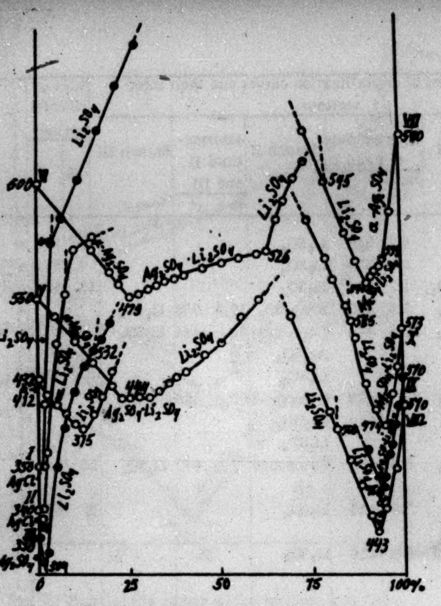

Fig. 4. Internal sections I—X.
I–65% Ag_2Cl_2 + 35% $Ag_2SO_4 \rightarrow Li_2Cl_2$; II–60% Ag_2Cl_2 + + 40% $Ag_2SO_4 \rightarrow Li_2SO_4$; III–47.5% Ag_2Cl_2+52.5% $Ag_2SO_4 \rightarrow Li_2SO_4$; IV–25% Ag_2Cl_2 + 75% $Ag_2SO_4 \rightarrow Li_2SO_4$ V–10% Ag_2Cl_2 + 90% $Ag_2SO_4 \rightarrow Li_2SO_4$; VI–5% Ag_2Cl_2 + 95% $Ag_2SO_4 \rightarrow Li_2SO_4$; VII–80% Ag_2SO_4 + 20% $Li_2SO_4 \rightarrow$ $\rightarrow Li_2Cl_2$; VIII–75% Ag_2SO_4 + 25% $Li_2SO_4 \rightarrow Li_2Cl_2$; IX–70% Ag_2SO_4 + 30% $Li_2SO_4 \rightarrow Li_2Cl_2$; X – 60% Ag_2SO_4 + 40% $Li_2SO_4 \rightarrow Li_2Cl_2$; M = α-Ag_2SO_4; N = β-Ag_2SO_4.

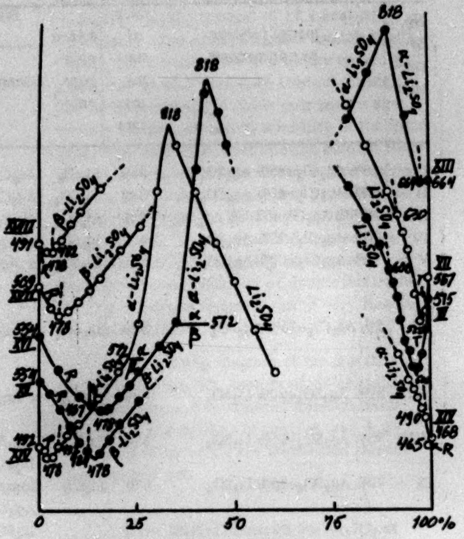

Fig. 5. Internal sections XI—XIX.
XI–50% Ag_2SO_4 + 50% $Li_2SO_4 \longrightarrow Li_2Cl_2$;
XII–40% Ag_2SO_4 + 60% $Li_2SO_4 \longrightarrow Li_2Cl_2$;
XIII–90% Li_2SO_4 + 10% $Li_2Cl_2 \longrightarrow Ag_2SO_4$;
XIV–50% Li_2SO_4 + 50% $Li_2Cl_2 \longrightarrow Ag_2SO_4$;
XV–25% Li_2SO_4 + 75% $Li_2Cl_2 \longrightarrow Ag_2SO_4$;
XVI–25% Ag_2Cl_2 + 75% $Li_2Cl_2 \longrightarrow Ag_2SO_4$;
XVII–50% Ag_2Cl_2 + 50% $Li_2Cl_2 \longrightarrow Ag_2SO_4$;
XVIII–60% Ag_2Cl_2 + 40% $Li_2Cl_2 \longrightarrow Ag_2SO_4$;
XIX–75% Ag_2Cl_2 + 25% $Li_2Cl_2 \longrightarrow Ag_2SO_4$.
R – Solid solutions (Li, Ag) Cl; T – $Ag_2SO_4 \cdot Li_2SO_4$.

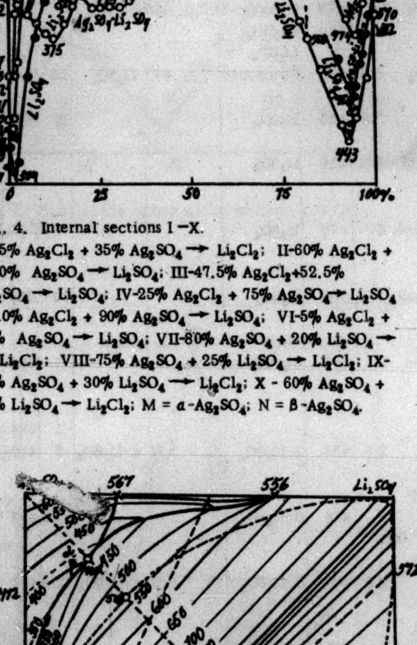

Fig. 6. Projection of isotherms on to the square of compositions.

The singular temperature maxima of all the sections are at the points of their intersection with the stable diagonal section. The results of measurements are generalized in the form of a projection of the isotherms on to the square of compositions of the reciprocal system (Fig. 6). The positions of the invariant points, of the lines of joint crystallization of components, and of the lines demarcating the stratification region are represented in the form of projections of those points and of the lines of the ternary system Ag_2Cl_2–Li_2SO_4–Li_2Cl_2 on to the AgCl–LiCl side (Fig. 7) and of the lines of the ternary system Ag_2Cl_2–Li_2SO_4–Ag_2SO_4 on to the Li_2SO_4–Ag_2SO_4 side (Fig. 8).

On the projections are also represented the three-phase and four-phase monotectic equilibrium (ab and cd in Fig. 7 and ab in Fig. 8) and the polymorphic transformation of lithium sulfate (broken line).

We see from Fig. 6 that the system consists of eight fields of crystallization: *a*, β- lithium sulfates occupying 75.6%, *a*, β-solid solutions of [Ag, Li]Cl (15.3%); *a*, β-sulfates of silver (6.5%); compound $Ag_2SO_4 \cdot Li_2SO_4$ (2.2%) and silver chloride 0.4% of the total area of the square.

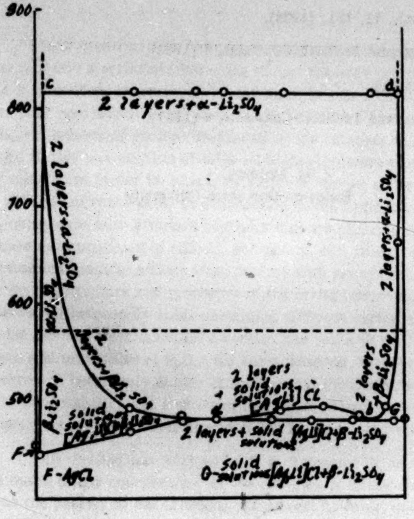

Fig. 7. Projection of the ternary system Ag_2Cl_2–Li_2SO_4–Li_2Cl_2 on to the AgCl–LiCl side.

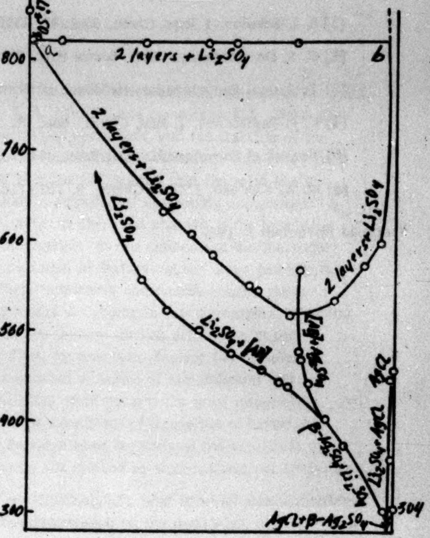

Fig. 8. Projection of the ternary system Ag_2Cl_2–Li_2SO_4–Ag_2SO_4 on to the Li_2SO_4–Ag_2SO_4 side.

The stable diagonal section Ag_2Cl_2–Li_2SO_4 cuts the square of the reciprocal system at two ternaries: Ag_2Cl_2–Li_2SO_4–Ag_2SO_4 with a ternary eutectic melting at 290°. In the same system is found the transient compound $Ag_2SO_4 \cdot Li_2SO_4$, Ag_2Cl_2–Li_2SO_4–Li_2Cl_2 with solid solutions of [Ag, Li]Cl. The region of stratification occupies 65.2% of the total area of the square of compositions. Its greater part lies in the lithium sulfate field and only a very minor portion in the field of solid solutions of [Ag, Li]Cl. On the line of joint crystallization of the compounds in question, a four-phase monotectic process takes place in the stratification region at 478°.

The compound $Ag_2SO_4 \cdot Li_2SO_4$, which is congruent on the outer side, becomes incongruent inside the system with a "transition" point at 412°; it decomposes on melting under the influence of silver chloride and of the stratification region. It does not enter into the composition of the phase complexes of the solidifying melts.

SUMMARY

1. The ternary reciprocal system of the chlorides and sulfates of lithium and silver has been investigated in melts by the visual-polythermic method of physicochemical analysis. The system belongs to the singular irreversibly reciprocal type of system with stratification in melts, i.e., to the third class of the classification of A.G. Bergman and Dombrovskaya.

2. The reciprocal system Li, Ag ‖ Cl, SO_4 is characterized by a well-marked singularity with a sharp unilateral shift of equilibrium in the direction of silver chloride and lithium sulfate due to the extremely limited reciprocal solubility of these salts in the melted state and to the high thermal effect of the reaction $Li_2Cl_2 + Ag_2SO_4 \longrightarrow Li_2SO_4 + Ag_2Cl_2$, which is equal to 17.80 kcal per equivalent.

3. The stable diagonal section is a singular plane in which intersection occurs of the isotherm and boundary of stratification of the ternary systems Ag_2Cl_2–Li_2SO_4–Ag_2SO_4 and Ag_2Cl_2–Li_2SO_4–Li_2Cl_2 at an acute angle.

4. The investigation of the reciprocal system Li, Ag||Cl, SO_4 has provided further support for the hypothesis that stratification in the fused state in the majority of cases is the consequence of a differing structure of the outer electron shells of the ions and of the resultant sharp difference in their polarization characteristics and in the physicochemical properties of the components of the stable pair.

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A STUDY OF PHOSPHOMOLYBDIC AND SILICOMOLYBDIC COMPLEXES IN SOLUTION

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Many investigations have been made of the composition and structure of heteropoly compounds in the solid state; recently a series of interesting studies has been published by E. A. Nikitina and co-workers [1]. These give little information, however, about the equilibria in solution, the formation conditions, and the stability of the heteropoly compounds in solution. B. V. Nekrasov [2] considers the interaction of caustic alkali with heteropoly acids as a process of gradual breakdown of the complex acid; E. A. Nikitina [3] assumes that the solid phase formed in this way consists of solid solutions (limitedly saturated and unsaturated) of heteropoly compounds. A very significant factor for characterization of the use of heteropoly acids in chemical analysis is the formation and stability of these acids in dependence on the hydrogen ion concentration. In this connection the molybdic acid complexes with different central atoms are characterized by a number of features which make possible the separate determination of silicon, phosphorus, etc. in mixtures. These heteropoly compounds exhibit these well-marked specific effects when reacted with various anions which bind molybdenum into a complex. Existing data for the structure and properties of the crystalline compounds do not account for this difference in the properties of heteropoly acids containing different central atoms. Thus, for example, Pauling [4] considers that the central atom occupies a certain free space in the lattice composed of atoms of molybdenum and oxygen and molecules of H_2O. We know, however, that the central atom often governs the most important properties of heteropoly acids. It is clear that the characteristics of the conditions of formation of heteropoly acids, their stability and a series of individual properties can only be established by study of the equilibria of formation in solution. This approach can be made most effectively by the method of physicochemical analysis.

This method was adopted by I. V. Tananaev [5] in a study of silicomolybdic acid in which determinations were made of the composition of the complex in solution and of the dependence on the molybdate concentration and on the acidity of the solution. Tananaev, however, only studied equimolecular mixtures in which equality existed between the sums of the concentrations of the three components: sum of SiO_2, MoO_3 and H_2SO_4 = 0.025 mole/l. In the practice of colorimetric analysis, however, considerably larger excesses of acid and molybdate are employed.

The objective of the present investigation was the study of the equilibria, formation conditions and stability of phosphomolybdic and silicomolybdic acids in solutions; the principal method of investigation was physicochemical analysis.

General characterization of the conditions of equilibrium in the system phosphate (silicate)-molybdate-acid. We applied physicochemical analysis to the investigation of the equilibrium (reversible) systems. It may be noted, however, that certain properties of the solutions of the reacting components clearly indicate irreversibility of the reactions in certain conditions.

The state of molybdenum in acidified solutions of ammonium molybdate has hitherto not been adequately studied. Investigation of various characteristics of molybdic acid solutions (depression of freezing point, diffusion coefficients, dialysis, etc., [6,7,8]) has revealed the presence in acid solutions of various forms of polymerized molybdic acid ions. Thus, for instance, simple ions of MoO_4^{--} are found in molybdate solution in an alkaline medium and when the pH is reduced to 6.5. Further drop in the pH from 5.0 to 1.5 leads to formation of hexamolybdates, and still greater acidification leads to dodecamolybdates. At the same time the possibility is not excluded of formation of trimolybdate ions when the pH of the solutions is 6.5-5.0. At the same time there are various theories of the nature of the coordinated groups in heteropoly acids; thus the composition of phosphomolybdic acid, as we know it, is represented by the formula $H_7[P(Mo_2O_7)_6]$ or $H_3[P(Mo_3O_{10})_4]$. Consequently phosphomolybdic acid may exist in equilibrium with dimolybdate or trimolybdate ions. Since a higher degree of polymerization of molybdate is probable in strongly acid solutions, while the speed of depolymerization is unknown, the formation is possible of systems which are not in equilibrium, and the method of physicochemical analysis may prove to be inapplicable.

We know also that due to the colloidal character of solutions of silicic acid, the conditions of formation and breakdown of silicomolybdic acid exhibit a series of peculiarities [9]. We know that in the colorimetric determination of silicon in presence of phosphorus, use is made sometimes of strongly acid solutions, the silicomolybdate complex being stable while the phosphomolybdic complex decomposes. In other cases the test solution is first acidified and after a short period addition is made of molybdate; in these conditions a silicomolybdic complex is not formed. Consequently in the case of solutions of silicomolybdic complexes the absence of equilibrium may result (apart from the factors mentioned above) from the colloidal character of silicic acid in solutions. This fact clearly calls for a preliminary study of the general characteristics of equilibrium in the system.

The following starting solutions were used: 1) Solution of ammonium molybdate containing 0.1 mole MoO_3 per liter; 2) 0.1 molar solution of sodium silicate or sodium phosphate; 3) 0.2 N nitric acid solution. These solutions were mixed in various ratios and in various orders with variation of the period between mixing of two components and introduction of the third component. Mixing of the three components was followed by determination of the optical density of the solutions after intervals of 10 minutes and 1, 4 and 24 hours.

Omitting the experimental details, we may note the following results: In most cases the optical density of the solution was identical for solutions of phosphomolybdic complexes, regardless of the order of mixing and of the time within the limits of the following concentrations. $[PO_4^{---}] = 2\cdot10^{-4}$, $[MoO_4^{--}]$ from $24\cdot10^{-4}$ to $324\cdot10^{-4}$ and pH of 0.7 to 2.0. The experimental data consequently supply evidence of sufficiently complete reversibility of the system.

The data for solutions of the silicomolybdic complex revealed poor reversibility of the processes and a considerable dependence of the optical density of the solutions on the order of mixing and on the period of standing. The most reproducible results were obtained in the following conditions: To a solution of silicate was added distilled water, followed by the required amount of acid, and immediately after mixing, this was followed by ammonium molybdate solution. This order of mixing of the reacting substances was also followed in the experiments described in the subsequent sections of this paper. Approximately the same optical density was obtained by adding the molybdate to the acidified silicate and holding for a short period; also by adding the silicate solution to the acidified molybdate solution. But if the silicate and molybdate solutions were first mixed together and then the acid added, the results were poorly reproducible. The optical density of all the solutions changes with time. At the start the color is intensified but afterwards it weakens, due to gradual irreversible decomposition of the silicomolybdic complex with formation of colloidal silicic acid in a form that does not react with molybdate. In Table 1 are presented some experimental results. The solutions were prepared as described above. The color intensity was determined by comparison of the test solutions with a borax-containing K_2CrO_4 solution.

TABLE 1

Silicate Concentration: $2\cdot10^{-4}$ ml

Molybdate conc.	$24\cdot10^{-4}$			$124\cdot10^{-4}$			$224\cdot10^{-4}$			
pH of solution	2.0	1.3	0.7	2.0	1.3	0.7	2.0	1.3	0.7	0.3
Period of standing	Color corresponds to a solution containing following amount of chromate (in mg/l)									
10 minutes.	30	8	0	70	85	26	70	70	60	2
1 hour. . . .	38	18	1	70	85	58	75	75	75	4
4 hours . . .	34	22	1	56	80	80	56	60	70	6
24 hours . .	18	20	1	40	60	60	30	44	56	12

The experimental results show that with increasing acidity of the solution there is an increase in the period necessary for maximum formation of the colored complex. Increasing concentration of molybdate cuts down this period but does not bring about complete stability of the complex; in all cases the complex is appreciably decomposed at a pH of 2 to 1.3 after 24 hours.

The influence of temperature must be considered in connection with the question of equilibrium in the system. Solutions were heated in test tubes to 60° and they were compared in the hot state with standard chromate solutions. The color intensity of solutions of phosphomolybdic complex increases 3-10 times at 60° (depending on the Mo/P ratio) in comparison with the same solutions at 20°; after cooling to 20° the color intensity of the solutions again falls to the initial value. The color intensity of solutions of the silicomolybdic complex in some cases also increases when heated. On cooling, however, the intensity does not fall to the original value and the period of stability of solutions of silicomolybdic complex is shortened.

Strickland [10] observes that the optical density of freshly prepared solution of silicomolybdic acid falls by approximately a factor of 2 after 24 hours. He attributes this to formation of an isomer of unknown structure. In an examination of solutions of silicomolybdic complex at various values of pH and various concentrations of excess molybdate, we did not observe any stable products of decomposition or isomerization of silicomolybdic complex in solution.

The above results show that the processes are reversible in solutions of phosphomolybdic complexes; conversely, irreversible processes are observed in silicomolybdic solutions, associated with passage of silicic acid into the colloidal state. Consequently physicochemical analysis, when applied to the formation of the silicomolybdic complex, can only give approximate results. In all cases the solutions containing a molar ratio of phosphorus (or silicon) to molybdenum of 1:12 have a much lower optical density than solutions with a large excess of molybdate. This fact points to appreciable dissociation of the complexes.

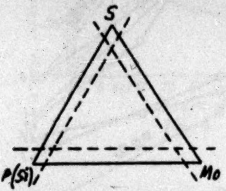

Fig. 1.

Examination of equimolecular mixtures. Determination of the composition of the complex in solution when the stability is low (appreciable dissociation) is most conveniently carried out by a study of the properties of mixtures containing a constant total of molar concentrations of reactants. Phosphomolybdic and silicomolybdic complexes are formed by reacting phosphate (or silicate) with molybdate in an acid medium. Nitric, hydrochloric or sulfuric acids, however, do not enter into the composition of the complexes according to the available data; nor do hydrogen ions enter into the coordination sphere since heteropoly acids are strong acids. Evidently a certain degree of acidity of the solution influences the degree of polymerization of the molybdic acid ion. We therefore considered it would be expedient to perform some series of experiments at various pH values, but with maintenance only of a constant sum of the phosphate (or silicate) and molybdate while keeping the pH of the solutions constant. • On this basis a study was made of complexes in a system of two reactants in solution. The system may be represented by a triangle of composition: The central ion [P(Si)], the coordinated ion (Mo) and the solvent (S) (Fig. 1). Equimolecular mixtures correspond to sections of the triangle of composition parallel to the side P (Si)–Mo.

Experiments for various equimolecular mixtures containing an identical molar ratio of the coordinated ion to the central ion Mo/P(Si) corresponded to sections through the apex of the triangle and the appropriate point on the side P(Si)–Mo.

Other sections are described in later parts of this paper. The usual form of graphical representation of the results of physicochemical analysis are unsatisfactory in the present case because the composition of the obtained colored compounds diverges sharply from the 1:1 ratio. Consequently, on the ordinates we have marked directly the P/Mo ratio in the range of 1 to 50. By this means the middle of the abscissas corresponds not to the ratio P:Mo = 1:1 (as in the usual diagram) but to the ratio P:Mo = 1:25.

In Fig. 2 are shown the results of several series of experiments. Constancy was maintained of the sum of the molar concentrations of phosphorus and molybdate in each series, and the acidity of the solution was also held at a constant value. Acidification was effected with sulfuric acid; the normality of the solution in terms of sulfuric acid is specified for each series of experiments below Fig. 2. The optical density was measured on a FM photometer using a light filter with an effective wave length of 465 mμ.

Examination of the plots on the diagram shows that in each series of experiments there is a maximum in the optical density, which indicates the formation of one colored complex compound in the given series. The maximum in each series is observed at a different molar ratio of phosphate to molybdate in solution. For those series of experiments in which the acidity was $[H^+]$ = 0.03-0.085 N, the maximum of optical density corresponds to the ratio P:Mo = 1:24, at an acidity of 0.2 N it corresponds to P:Mo = 1:19 (the optical density at P:Mo = 1:12 and 1:24 differ slightly from the maximum); in weakly acid solutions (0.01 N) the maximum of optical density corresponds to P:Mo = 1:12. The correlation of the maximum of optical density of solutions with series of solutions of differing ratios of P:Mo points to formation of complexes of different compositions.

• Concerning the suitability of physicochemical analysis for the investigation of such systems, we may note that the condition of equimolarity of a series of solutions is also to some extent arbitrary in view of the undoubted (if not accurately known) polymerization of molybdate. Consequently, apart from other reasons, we believe it is necessary not to limit ourselves to the examination of equimolecular solutions but to also investigate other ratios (see the later sections).

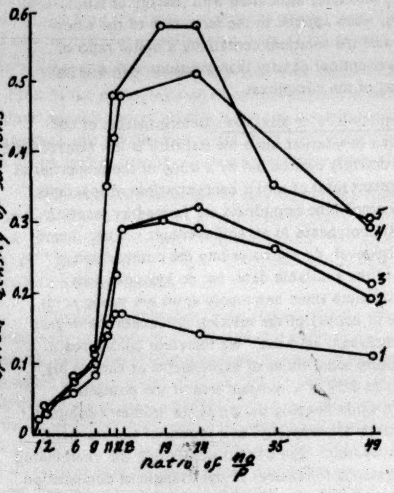

Fig. 2. Normality of the solution with respect to sulfuric acid. 1) 0.01 N, 2) 0.02 N, 3) 0.085 N, 4) 0.03 N, 5) 0.07 N.

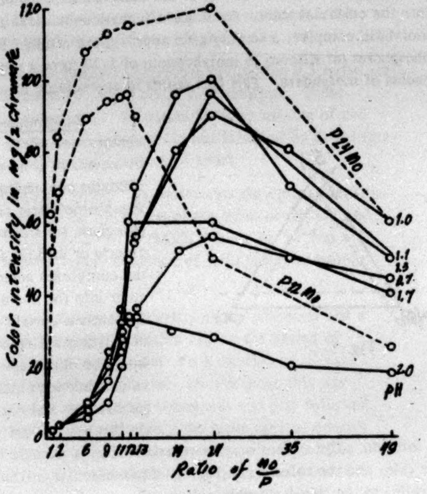

Fig. 3.

The optical density is seen to drop sharply in all the series of experiments with a P: Mo ratio greater than 1:12, indicating the formation in these experimental conditions of a colorless complex compound containing less than 12 atoms of molybdenum per atom of phosphorus.

In Fig. 3. are plotted the results of some series of experiments, with a constant sum of concentration of molybdate and phosphate in solution of $125 \cdot 10^{-4}$ mole/l. The various series differed only in respect to the pH of the solution. The pH values of individual series ranged from 0.7 to 2.0. Nitric acid was the acidifying agent. The color intensity of the solutions was measured by comparison with a series of standards consisting of potassium chromate and borax. In the diagram the curves corresponding to the color intensity of the experimental solutions are represented by solid lines. The broken lines represent the color theoretically calculated for the case of complete bonding of phosphate in complex compounds containing 12 to 24 atoms of molybdenum per atom of phosphorus.

Inspection of the curves reveals, as in the above-described experiments, that at higher acidities (pH = 0.7-1.3) the maximum color of the solutions occurs at ratios of P: Mo = 1:24, and that at pH = 2.0 the color maximum occurs at a ratio of 1:12. The greatest distance between the solid and the broken lines occurs in the portion of the diagram to the left of the maximum of intensity, which confirms the formation of a colorless complex when there is excess of phosphate in the solution. The distance between the solid lines corresponding to the experimental data for pH values of 0.7 to 1.3 and the broken line corresponding to the color theoretically calculated[*] for the case of complete binding of phosphate into the colored complex with a ratio of P: Mo = 1:24 decreases with increasing molybdate content. A similar dependence is found for the curves at pH = 2 for the theoretically calculated color in the condition of complete bonding of phosphate in the colored complex with a ratio of P: Mo = 1:12. Hence with increasing excess of molybdate in the solution, no new complexes are formed, and more complete linking of phosphate to the colored complex is observed.

The following main conclusions can be drawn from the described experiments. The maximum of optical density of equimolecular mixtures of phosphate and molybdate at a pH of about 2 is observed with a ratio of

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[*] Calculation was performed on the basis of the value of the molar absorption coefficient measured in presence of a considerable excess of molybdate.

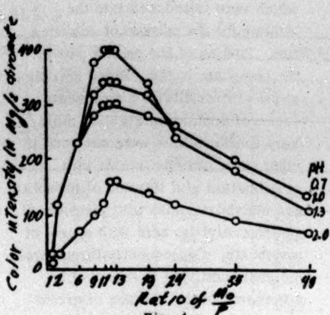

Fig. 4.

P: Mo = 1:12, and in a series of cases with pH of 0.7 to 1.3 the maximum is at P: Mo =1:24. The latter results justify the inference that in certain conditions a more complex phosphomolybdic acid, containing 24 atoms of molybdenum per atom of phosphorus, is formed. The formation of such compounds may be correlated with the higher degree of polymerization of molybdate in acid solutions. Since the degree of polymerization of molybdate is not known at present with sufficient reliability, the above results may be regarded as preliminary (see also the observation on p. 391). It is significant, however, that in the system silicate-molybdate (see below) the maximum of optical density in equimolecular mixtures corresponds only to the ratio Si: Mo = 1:12. Moreover, as was remarked above, the optical density sharply increases in the system phosphate-molybdate with rising temperature. At the same time, the position of the optical density maximum also shifts in such a manner that at a temperature of 60° in all cases the maximum corresponds to the ratio P: Mo = 1:12. Fig. 4 shows the data[*] obtained for equimolecular mixtures at 60°.

Results obtained for the system silicate-molybdate are presented in Fig. 5. They confirm the conclusions of I. V. Tananaev [5] about the formation in solution of a colored compound with a ratio of Si: Mo = 1:12. In view of the above data for the dependence of the color on the duration and order of mixing of the solutions, experiments were carried out in the following way: Acid was added to the dilute solution of silicate, mixing was performed and immediately after that the molybdate was added. The optical density of the solutions was measured after 10 minutes and 1, 4 and 24 hours.

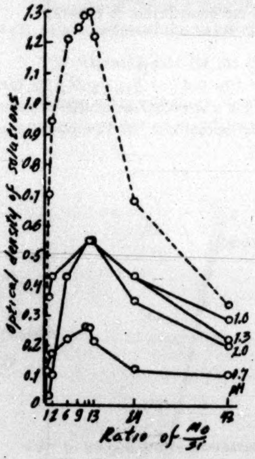

Fig. 5.

The maximum of optical density is much lower in solutions of the silicomolybdic and of the phosphomolybdic complexes than the value calculated for the conditions of full binding (see the broken and solid lines in Figs. 3 and 5). This signifies appreciable dissociation or partial irreversible decomposition of the complex in the absence of excess of molybdate. This inference was checked by experiments using a solution of phosphomolybdic acid previously isolated in the pure form. When a 10^{-3} molar solution of the acid was twice diluted, the optical density fell by a factor of 3, which confirms the fall in the number of absorbing light centers on dilution. The same result was obtained in the case of presence of sulfuric acid in a phosphomolybdic acid solution. Introduction of excess of acidified solution of molybdate intensifies the optical density of the solutions.

Concerning the effect of pH, the foregoing data make it clear that at pH = 2 the formation of colored compounds is intensified, but at higher acidities (pH = 0.7 and less) the color of solutions of phosphomolybdic acid is less intense. A certain optimum acidity of solution is also observable with the silicomolybdic complex but the dependence is a more complex one due to the irreversibility of the process.

Study of solutions with constant concentration of the central ion and variable concentration of the coordinated ion. These solutions correspond to the section of the triangle of composition along lines parallel to the side S-Mo. This section permits the determination of the degree and character of the effect of excess of the coordinatable ion which is the reactant in the conditions of colorimetric analysis. Some data for the phosphomolybdic complex are given in Table 2.

The results show that with increasing concentration of molybdate the color intensity increases but subsequently remains nearly constant, this stage corresponding to complete binding of the phosphate in the colored complex. At a pH of about 1.7-2.0 with a very large excess of molybdate, the color weakens, evidently due to secondary processes developed under the influence of anions of the acids which were introduced into the solution for the purpose of acidification. Binding of the greater part of the phosphate in the colored complex at pH = 1 necessitates a molybdate excess of approximately 0.01 mole/l. Very similar results were obtained in other series of experiments with acidification of a solution of phosphate and molybdate, also with mixtures of phosphomolybdic acid with excess of molybdate. Consequently the phosphomolybdic complex is appreciably dissociated in the absence of excess of molybdate.

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[*] The data were obtained by comparing the heated solutions with standard solutions of chromate (these were not heated), because measurement of optical density at 60° is inconvenient with the help of a photometer.

TABLE 2

Prep. No.	Molar conc. of molybdate $C_{Mo}\cdot 10^4$	Molar conc. of phosphate									
		$C_P = 1.0\cdot 10^{-4}$					$C_P = 2.0\cdot 10^{-4}$				
		pH of solution									
		2.0	1.7	1.3	1.0	0.7	2.0	1.7	1.3	1.0	0.7
		corresponds to color of chromate (mg/l)									
1	48	8	14	16	10	–	12	24	24	16	8
2	88	8	14	20	24	–	16	30	36	38	28
3	124	8	14	24	22	–	16	28	40	44	40
4	224	8	12	24	28	28	12	24	36	48	50
5	324	6	8	24	26	26	12	16	38	48	52

For the characterization of the stability of heteropoly acids, interest attaches to determination of the equilibrium constant of the reaction between the central and the coordinatable ion. This determination cannot be performed accurately since the degree of polymerization of molybdate in solution is unknown. On the basis of experimental data we can calculate the concentration of phosphate bound into the complex ($[PO_4Mo_x]$) from measurements of the optical density, also the concentration of molybdate ($[Mo_{free}]$) not bound to the colored complex and that of the phosphate ($[PO_{4free}]$) not bound to the colored complex; the last two magnitudes are calculated from the difference between the total concentration of the respective ions and the concentration of the colored complex. Such a calculation, however, must be regarded as approximate due to the following two facts: a) The phosphate and molybdate not bound into the colored complex can partly exist in solution in the form of colorless complexes; b) the molybdate not bound into the complex is present in a polymerized form; thus, if the total number of coordinated atoms of molybdenum is equal to $x = n \cdot m$*, then the equilibrium in general may be represented by the scheme**;

$$PO_4Mo_{n\cdot m} \rightleftarrows PO_{4free} + n\,Mo_{n}. \qquad (1)$$

A study of the shift of equilibrium with changing concentration of molybdate can, evidently, only permit us to calculate the value of n, since this term determines the degree of influence of molybdate on the equilibrium shift of the formation of the colored complex.

In accordance with equation (1) we can write the equilibrium expression:

$$K_{complex} = \frac{[PO_{4free}][Mo_m]^n}{[PO_4\cdot Mo_x]} \qquad (2)$$

Putting (2) into logarithmic form, we get:

$$\log K_{complex} = n \log [Mo_m] + \log \frac{[PO_{4free}]}{[PO_4\cdot Mo_x]} \qquad (3)$$

Putting $\log K_{complex} = a$ (constant), we get:

$$n \log [Mo_m] = a + \log \frac{[PO_4\cdot Mo_x]}{[PO_{4free}]} \qquad (4)$$

The ratio $[PO_4\cdot Mo_x]:[PO_{4free}]$ is determined from experimental data and characterizes the degree of bonding of phosphate in the colored complex. This ratio depends on the concentration of the excess of molybdate; a p-fold change in the molybdate concentration results, in accordance with equation (2), in the ratio of bound to unbound phosphate changing by a factor of p^n; in this way we can calculate the magnitude of n, i.e., the coefficient in equation (1). This calculation is more conveniently performed on the basis of equation (4); if we plot (in identical scales) on the abscissas the values of $\log [Mo_{free}]$ and on the ordinates the values of $\log [PO_4\cdot Mo_x]/[PO_{4free}]$, then the tangent of the angle of slope will be equal to the value of n. Some experimental and calculated values are enumerated in Table 3.

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* Usually x = 12.

** Arbitrary symbols are introduced into this equation in order not to confuse the study of the equilibrium by any concepts on the basis of the study of the derived equation (1a) (see below).

TABLE 3

Expt. No.	Molar conc. of molybdate $C \cdot 10^4$	Molar conc. of phosphate $2 \cdot 10^{-4}$						
		pH = 1.0						
		corresponds to color of chromate (mg/l)	$[P_{bound}]$ $C \cdot 10^4$	$\frac{[P_{bound}]}{[P_{free}]}$	$[Mo_{free}]$ $C \cdot 10^4$	$\log \frac{[P_{bound}]}{[P_{free}]}$	$\log [Mo_{free}]$	$-\log K_{complex}$
1	48	16	0,66	0.49	40.08	−0.31	−2,40	9,29
2	88	38	1.58	3.76	69.04	0.58	−2.16	9,22
3	124	44	1.83	10.8	102.04	1,03	−1.99	8,99
4	324	48	2.00	−	−	−	−	−
5	48	14	0.63	0.46	40.44	−0.34	−2.39	9.22
6	88	36	1.63	4.40	68.44	0.64	−2.17	9.32
7	124	40	1.82	10.10	102.16	1.00	−1.99	8.96
8	324	44	2,00	−	−	−	−	−
9	48	12	0.60	0.43	40.80	−0.37	−2.39	9.19
10	88	32	1.60	4.00	68.80	0.60	−2.16	9.24
11	124	36	1.80	9.00	102.40	0.95	−1.99	8.91
12	324	40	2.00	−	−	−	−	−

Experiments 1 to 4 were performed in presence of nitric acid, 5 to 8 in presence of hydrochloric acid, and 9 to 12 in presence of sulfuric acid.

The data of Table 3 show that a slight increase in molybdate concentration sharply shifts the equilibrium of (1). Calculation of the value of n by the above procedure gives 3.7 and 4.3 (see Fig. 6).

The presented data for the value $n \approx 4$ to some extent are consistent with the formula for phosphomolybdic acid $H_3[P(Mo_3O_{10})_4]$, and not with the formula $H_7[P(Mo_2O_7)_6]$. If we assume that dissociation of the colored complex yields free phosphate and molybdic anhydride with a polymerization factor of 3 (m = 3), then on the basis of study of the equilibrium we may express equation (1) in the form*:

$$P(Mo_3O_{10})_4^{---} \rightleftarrows PO_4^{---} + 4(MoO_3)_3. \qquad (1a)$$

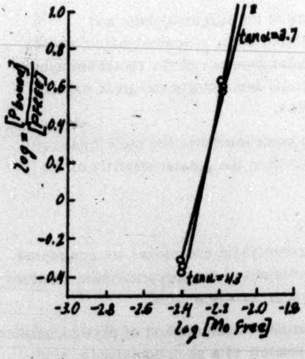

Fig. 6.

The last column of Table 3 contains the negative logarithms of the equilibrium constant of the phosphomolybdic complex calculated on the basis of n = 4. The equilibrium constants calculated on this assumption are sufficiently constant with a fairly large change of molybdate concentration as well as of the pH of the solution (in other experiments). On the basis, therefore, of the above data we can assume for a pH of 1.0 that:

$$K_{complex} = \frac{[PO_4^{---}][(MoO_3)_3]^4}{[P(Mo_3O_{10})_4^{---}]} = 5.6 \cdot 10^{-10}.$$ The mean value is given.

This value enables us to calculate that bonding of phosphorus to the extent of 99% in the colored complex takes place at a concentration of $[Mo_{free}] = \sqrt[4]{K \cdot \frac{99}{1}} \approx 10^{-2}$. This result is in satisfactory accord with the preceding experimental data.

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* The state of molybdate in strongly acid solution has not been adequately studied. Consequently the formula $(MoO_3)_3$ must be considered an arbitrary expression of the state in which it exists in the dilute molybdic liquid. The above-described experiments permit the possibility of determination of only the coefficient 4, since the equilibrium of complex formation changes in dependence on the fourth power of the concentration of the excess molybdate. The polymerization factor of 3 has not been experimentally proved, and is merely an inference from the over-all composition of the complex (12 atoms of molybdenum per atom of phosphorus) and from the coefficient 4.

A considerable shift of equilibrium is likewise observed for the silicomolybdic complex on introduction of excess of molybdate; when this excess is about $8 \cdot 10^{-3}$ molar, the optical density becomes almost constant, i.e. there is substantially complete bonding of silicic acid in the colored complex. Some data obtained 1 hour after mixing of the initial solutions are submitted in Table 4.

Hence the general character of the dependence, and also the concentration, at which a colored complex is formed is roughly the same as for the phosphomolybdic complex, although the silicomolybdic complex is distinguished by less dissociation. Data are given below for the stability of the silicomolybdic complex in presence of excess of citric acid and phosphate ion. Due to the instability of the equilibrium of formation of the silicomolybdic complex, more detailed calculations were not undertaken.

Investigation of solutions with constant concentration of molybdate and varying concentration of the central ion of the complex and comparison of the stability of the complexes. These series of experiments corresponded to the section of the composition triangle along lines parallel to the S—P(Si) side. This section permits examination of the effect of excess of central ion.

Results of experiments with the phosphomolybdic complex showed that increasing concentration of phosphate in solution up to a P: Mo ratio of more than 1:12 was accompanied by weakening of the color intensity, which indicates a shift of equilibrium in the direction of formation of a colorless complex containing less than 12 g-atoms molybdate per g-ion phosphate.

TABLE 4

Expt. No.	Molar conc. of molybdate $C \cdot 10^4$	Molar conc. of silicate $2 \cdot 10^{-4}$				
		pH of solution				
		2.0	1.3	1.0	0.7	0.3
		light absorption of solution $\log \frac{I_0}{I}$				
1	24	0.14	0.08	0.02	0.00	–
2	48	0.26	0.26	0.17	0.02	–
3	88	0.26	0.29	0.29	0.10	–
4	124	0.26	0.29	0.29	0.21	–
5	224	0.21	0.29	0.29	0.26	0.03
6	324	0.22	0.29	0.29	0.29	0.04

A different effect of increasing silicate concentration in solution was observed for the silicomolybdic complex. With increasing silicate concentration the optical density of the solutions at first rises and then remains constant even with a ratio of Si: Mo considerably higher than 1:12. The data indicate that increasing concentration of silicic acid in solution does not lead to the formation of new complexes.

Apart from an examination of the conditions of formation of silicomolybdic and phosphomolybdic complexes in solution a study was also made (for the purpose of general characterization of the equilibrium) of the conditions of decomposition of the complexes under the action of reagents combined in the molybdate complex.

The experiments enabled us to obtain comparative data for the stability of the silicomolybdic and phosphomolybdic complexes. Addition of excess of phosphoric acid to the solution of the silicomolybdic complex does not lead to appreciable fall in the intensity of color of the solutions, whereas solutions of the phosphomolybdic complex are decolorized in similar experimental conditions. The obtained results demonstrate the great stability of the silicomolybdic complex in comparison with the phosphomolybdic complex.

Addition of citric acid to silicomolybdate solution does not change the color intensity; the same treatment decomposes the phosphomolybdic complex. The results of these experiments confirm the greater stability of the silicomolybdic complex in comparison with the phosphomolybdic complex.

SUMMARY

1. The equilibrium conditions in solution of phosphomolybdic and silicomolybdic complexes are considered. In solutions of the phosphomolybdic complex the processes are reversible. In solutions of the silicomolybdic complex irreversible processes are observed which are associated with the colloidal character of silicic acid.

2. The composition of colored phosphomolybdates in solution was examined by the method of physicochemical analysis. The obtained data indicate that in some conditions the formation is possible of a phosphomolybdic acid containing 24 atoms of molybdenum per atom of phosphorus. On heating to 60° only a compound with a P: Mo ratio of 1:12 is observed to be formed. For the silicomolybdic complex, in all conditions a compound with the ratio Si: Mo = 1:12 is formed.

3. The dissociation constant of the phosphomolybdic complex was determined; it was found that:

$$K_{complex} = \frac{[PO_4^{---}][(MoO_3)_3]^4}{[P(Mo_3O_{10})_4]} = 5.6 \cdot 10^{-10}.$$

4. An examination was made of the conditions of decomposition of the complexes under the influence of excess of hydrogen ions, phosphoric acid, and various complex-formers which bind molybdate. The silicomolybdic complex is characterized in all cases by a higher stability by comparison with the phosphomolybdic complex. Decomposition of the complex during standing of the solution is associated with irreversible formation of silicic acid.

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CRYSTALLINE ORGANOLITHIUM COMPOUNDS

ETHYLLITHIUM

T. V. Talalaeva and K. A. Kocheshkov

Existing methods of synthesis of organolithium compounds, with a few exceptions, yield solutions (more rarely suspensions) of the compounds. Usually the solution of the organolithium compound, containing (apart from RLi) lithium salts, alkyl halides and hydrocarbons, is brought into further reactions. A remarkably large number of diverse syntheses employing solutions of organolithium compounds has been described. The characterization (chemically or physicochemically) of organolithium compounds as such, however, necessitates isolation of the pure compound or its solution.

We were interested in the preparation of pure, crystalline ethyllithium (a most interesting compound for the study of exchange reactions with organoelement compounds) with the objective of developing methods of synthesis of pure aromatic or aliphatic-aromatic compounds of lithium.

Judging by the exchange reaction with tetraphenyllead, ethyllithium is the most active representative of the RLi series [1]:

$$C_2H_5Li > n\text{-}C_3H_7Li > n\text{-}C_4H_9Li > CH_3Li > C_6H_5C \equiv CLi.$$

It is also significant that ethyllithium may be recrystallized [2] or sublimed in high vacuum [3].

Up to now the synthesis of small quantities of ethyllithium, up to 0.7 g of crude material, has been performed in sealed vessels under nitrogen, by the action of lithium on diethylmercury; yield up to 93% [4].

$$(C_2H_5)_2Hg + 2Li \longrightarrow 2C_2H_5Li + Hg.$$

This method could not be widely adopted owing to the very high toxicity of the initial mercury compound.

Apart from this method, the literature contains a brief reference to the possibility of synthesis of a small quantity of ethyllithium (no indication of yield) by the action of lithium on ethyl chloride followed by removal of the solvent and isolation of the pure ethyllithium by sublimation in vacuum [5].

The method of preparation which we have developed for pure, crystalline ethyllithium is based on reaction of lithium with ethyl bromide followed by its separation from the lithium bromide; for this purpose advantage is taken of the differing solubility in benzene and isopentene (or hexane)

$$C_2H_5Br + 2Li \longrightarrow C_2H_5Li + LiBr.$$

We performed the reaction of ethyl bromide with lithium in a medium of isopentene (mixture of pentenes) with b.p. 27-36°; a grey-violet, heavy precipitate was obtained which consisted of a mixture of lithium bromide and ethyllithium. On addition of benzene, the isopentene was distilled off and the ethyllithium went over in the solvent (leaving a residue of lithium bromide and excess lithium). On cooling we obtained transparent solutions of ethyllithium with an ethyllithium yield of 65%. Subsequent distillation of a portion of the benzene enabled isolation of crystalline ethyllithium (yield 30-35%). After one recrystallization from hexane we obtained pure ethyllithium. All operations in the preparation and isolation of ethyllithium must be performed in an atmosphere of pure nitrogen. It should not be forgotten that ethyllithium inflames immediately when it comes into contact with air; flaming and carbonization of the preparation is observed even on sealing into tubes insufficiently carefully filled with nitrogen. The residues in the reaction flask after preparation of ethyllithium (lithium bromide, lithium, residues of C_2H_5Li solution) must be quickly decomposed (otherwise a fire may occur on access of air). Decomposition is effected by addition of benzene, then (carefully) of ethyl alcohol.

EXPERIMENTAL

Preparation of Crystalline Ethyllithium

a) Preparation of ethyllithium in an isopentene medium. Use was made of a 500 ml 3-necked flask connected by ground-glass fittings with a mercury seal, a reflux condenser, a dropping funnel and a nitrogen feed tube (the latter also serves for siphoning the solution) (Fig. 1). The dropping funnel, for equalizing the pressure, is connected through a three-way cock with the nitrogen tube. For purification of the nitrogen see reference 6. A broad funnel is inserted in the vessel (through the ground-glass connection for the condenser). 200 ml isopentene is poured in and a nitrogen stream is passed. A weighed amount of lithium (3.8 g or 0.56 g-atom) is beaten into a sheet about 1 mm thick, strips 5-7 mm wide are cut from it, purified from the oxide film, and quickly cut with scissors over a funnel in a stream of nitrogen into about 900-950 pieces.

The reflux condenser (attached to a drying system*) is then connected up and the apparatus is filled with nitrogen. In the dropping funnel is placed 21.8 g ethyl bromide (0.2 mole), about 1/8 of the total volume is run in, and the stirrer is started up.

The reaction starts spontaneously after 15-20 minutes of vigorous stirring at the boiling point of isopentene (in some cases the reaction only starts after 2-2¼ hours). Start of reaction is marked by spontaneous boiling, appearance of rapidly increasing turbidity, and then by a precipitate. Pieces of lithium sink to the bottom of the flask. In roughly 10 minutes after the start of the reaction the reaction mass becomes completely opaque. The color of the precipitate varies from light-grey to dark-grey; sometimes it is violet. The remainder of the ethyl bromide is added in small portions (uniformly) over a period of 3-3½ hours, after which stirring is continued with gentle boiling until bubbles cease to rise from the vicinity of the lithium particles (observation is made with heating suspended); this takes 1½ - 2 hours. The total duration of the reaction, starting from the addition of ethyl bromide, is 5-6 hours (in isolated instances up to 7-8 hours).

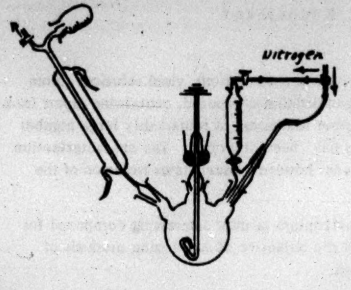

Fig. 1.

b) Preparation of benzene solution of ethyllithium. To the reaction mixture is added 100-120 ml benzene, heated to 30-35°. By turning the ground-glass connection the condenser is converted into a sloping one (Fig. 1) to which is attached a receiver (cooled with ice and water), and with continued stirring 170-180 ml isopentene is distilled off. At the conclusion of the distillation the stirrer is stopped and a small buret (100 ml) is attached for settlement of the solution; the buret is filled with nitrogen (Fig. 2). The tap connecting the condenser to the drying system is then closed, the siphon is lowered and, with continued heating, the solution with a considerable amount of precipitate is forced over with solvent vapors. The vessel containing the solution is disconnected and cooled at room temperature in a weak current of nitrogen. After standing for 12-14 hours there is obtained a perfectly transparent, colorless (sometimes slightly yellow) solution of ethyllithium. The volume of the solution is 90-100 ml; the concentration of the benzene solution of ethyllithium is about 1.25-1.28 N; yield of ethyllithium reaches 65%.

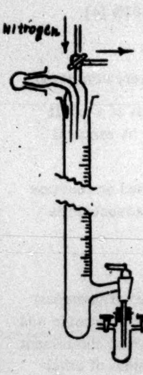

Fig. 2.

c) Isolation of crystalline ethyllithium. The apparatus for isolation of crystalline ethyllithium consists of a three-necked nitrogen tube (Fig. 3) of 120 ml volume, connected to a condenser and receiver and fitted with a filtration device [7]. Through the apparatus is passed about 8-10 volumes of nitrogen (in relation to the volume of the apparatus). The tap of the settling buret is joined to the nitrogen tube by means of a length of thick-walled rubber tubing; the buret is connected by a three-way cock with the nitrogen-supply system, and the transparent benzene solution of ethyllithium is run into the nitrogen tube. The upper exit is then closed (Fig. 3), a gentle stream of nitrogen is run through the condenser; and about 50-60 cc of benzene is distilled off. To the residue in the nitrogen tube is added 20 ml dry isopentene and the mixture is cooled with ice and salt. The separated crystals are removed from the sides and stirred, the lumps being crushed with a curved rod passed through the upper end of the nitrogen tube; the mass is then filtered on a porous glass filter [7], washed 3-4 times with dry pentane and dried (with passage of nitrogen and heating to 40-50°) for 30 minutes. For filtration and charging into ampoules under nitrogen, see reference 7.

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* Tubes containing phosphorus pentoxide, calcium chloride and sulfuric acid.

Use is made for analysis of thin-walled ampoules into each of which is introduced about 0.1-0.05 g substance (see below respecting analysis of crystalline ethyllithium). The yield of crystalline ethyllithium is about 2.5-2.3 g or 35-33%.

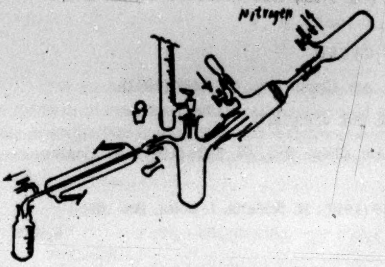

Fig. 3.

Ethyllithium is obtained in the form of a perfectly white, crystalline powder with m.p. 95° (with decomposition; determined in a capillary filled with nitrogen). The literature reports m.p. about 90° with decomposition [8].

Found %: Li 18.94, 19.00. C_2H_5Li.
Calculated %: Li 19.33.

After recrystallization from n-hexane, found %: Li 19.10, 19.16.

Ethyllithium readily dissolves in boiling benzene and hexane; on cooling it readily forms supersaturated solutions. Solubility in pentane (b.p. 28-38°); about 1 g ethyllithium is contained in 100 g solution at 18° (approximately 0.2 N solution); in isopentene (b.p. 27-35°) about 3 g ethyllithium is contained in 100 g solution at 16° and about 2 g ethyllithium at 0°; in hexane (b.p. 69°) at 55°. 100 g solution contains about 9.5 g ethyllithium, and at 18° the ethyllithium content is about 6 g; in benzene: at 16° 100 g solution contains about 7 g ethyllithium (the solution is approximately 1.66 N). The solubility in absolute ether at 18° is very high.

The yield of crystalline ethyllithium attains values of 10-20% when preparation is carried out in the same conditions in a medium of pentane.

Preparation of Ethyllithium in Ether Solution Followed by Transfer to Benzene Solution

The previously described all-glass apparatus (Fig. 1) is used. Into the flask are introduced 130 ml absolute ether and 4 g (0.57 g-atom) thinly sliced lithium (see above). The first portion of ethyl bromide is run in with stirring; vigorous boiling starts. The flask is lowered into ice water and the ethyl bromide is run in at such a speed that the vigorous boiling of the ether does not cease; this requires a period of 20 minutes. , 21.8 g ethylbromide (0.2 mole) is introduced in all. Addition is next made of 120 ml dry benzene, the condenser is turned into the sloping position and the ether is distilled off with uninterrupted stirring. The solution is dark-grey (nearly black); with progressive distillation of the ether a white precipitate forms. The volume of distillate is about 130 ml. The warm solution is siphoned into the buret under nitrogen for the purpose of settlement (Fig.2). After about 30 minutes the solution is nearly transparent. For complete clarification it is left to stand overnight. Analysis of the solution gives an ethyllithium/lithium bromide ratio of approximately 20:3. When concentrated under nitrogen ,the solution deposits a precipitate containing ethyllithium and lithium bromide in the ratio of 10:7, while the filtrate contains these substances in the approximate ratio of 7:1. It was not possible to isolate pure, crystalline ethyllithium by this method. The obtained benzene solution of ethyllithium may be utilized for further reactions.

Analysis of Organolithium Compounds

The greatest difficulty in the analysis of isolated organoalkali compounds is the weighing out of the readily oxidized and for the greater part readily inflaming compound. A dry ampoule is., therefore, first filled with nitrogen via a capillary and then closed with a piece of thickwalled elastic rubber tubing plugged with a glass rod. In the instant of weighing the sample (e.g. 0.1-0.15 g ethyllithium or 0.3-0.4 g phenyllithium) the ampoule is quickly connected (in a countercurrent of nitrogen) with an apparatus for filtration and drying of isolated organolithium compounds [9]. The tap connecting with the nitrogen supply is then closed and the ampoule is sealed. Thin-walled ampoules are used for analysis.

The sealed ampoule is placed in a thick-walled Bunsen flask (volume 500 ml) closed with a rubber stopper through which is passed a glass rod reaching to the bottom. 25-30 ml pure, dry benzene is run into the flask which is then filled with nitrogen; the ampoule is crushed by a swift movement. Ethyllithium goes into solution (phenyllithium becomes wetted with benzene). With the stopper slightly loosened, addition is made of 5 ml absolute alcohol and the mixture is shaken before adding 50-100 ml water. Titration is performed with 0.1 N sulfuric acid using phenolphthalein. Nitrogen is passed through the side tube of the flask during the analysis.

For the analysis of ethyllithium solutions it proved convenient to employ small conical flasks provided with two taps for passage of nitrogen (Fig. 4). Into 3-4 small flasks was first introduced a small quantity of benzene (otherwise the introduction of the ethyllithium solution would result in violent sputtering against the walls), the flasks were stoppered, linked together in series, and a dry nitrogen stream passed through for 10-15 minutes. After that, samples of 1-2 ml were quickly run in from the settling buret (Fig. 2) and decomposed and titrated in the usual manner [6,10].

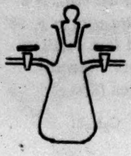

Fig. 4.

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* See Consultants Bureau translation.

CHARACTERIZATION OF PHTHALIMIDINEACETIC ACID

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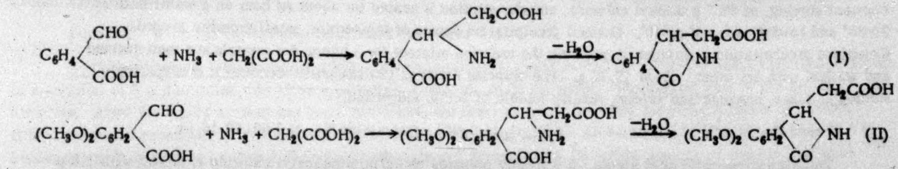
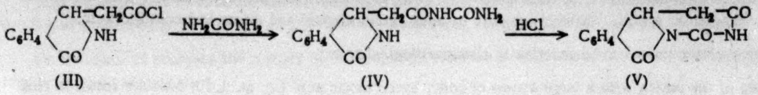
The method developed in our laboratory for the preparation of β-amino acids [1] was extended in 1930 to the synthesis of dimethoxyphthalimidineacetic acid [2] and in 1944 to that of phthalimidineacetic acid [5]. In these investigations it was shown that reaction of aromatic o-aldehyde acids with malonic acid in presence of alcoholic ammonia yields chiefly phthalimidineacetic acid (I) or its corresponding dimethoxy derivative (II)



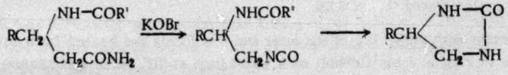
In our investigation we have attempted a more detailed study of the properties of phthalimidineacetic acid (I). With this objective we prepared its ethyl ester amide and ureide, and carried out experiments on the preparation of the corresponding complex dihydrouracil from the ureide of the acid according to the scheme:



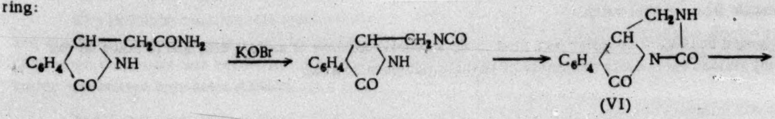
In studying these reactions it was found that the chloride of phthalimidineacetic acid, readily prepared in good yield (96%), condenses with urea to form the corresponding ureide (IV). This compound, however, does not undergo ring closure, and the complex tricyclic system (V) could not be obtained. In all the experiments either the ureide was recovered unchanged or the original phthalimidineacetic acid (I) was formed.

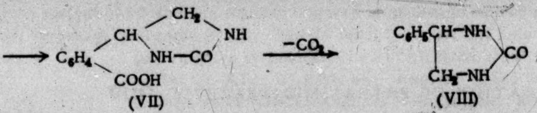
Attempts to obtain the ureide of phthalimidineacetic acid by the action of urea on the ethyl ester of the acid in presence of sodium ethylate led to the isolation of a mixture of amide and ureide, and no ring closure was detected.

For the purpose of further characterization of phthalimidineacetic acid, a study was made of the reaction of the acid amide with KOBr in the conditions of the Hofmann reaction. Similar investigations with β-amino acid amides were frequently carried out successfully by Kanevskaya [4] and in our laboratory [5], and in all cases it was established that the main reaction product is the corresponding imidazolone derivative formed via the isocyanate



In the case here studied, it transpired that the reaction proceeds in a somewhat more complicated manner; in place of the anticipated anhydride of phenylimidazolone carboxylic acid (VI), which is also a tricyclic system, there is obtained the phenylcarboxy derivative of the imidazolone (VII), apparently due to rupture of the lactam ring:





(VII) (VIII)

The structure of the phenylimidazolone carboxylic acid was established by a study of its properties, by the elementary analysis, and by the result of decarboxylation. The latter reaction proceeds either through simple repeated fusion of the compound, or, better, by heating a mixture of the phenylimidazolone carboxylic acid and naphthalene at 200-220°. The resultant product (VIII) was identical in all respects with the phenylimidazolone prepared by Kanevskaya [4] and Kiseleva [5].

EXPERIMENTAL

Phthalimidineacetyl chloride. Gradual addition is made to 11.5 g phthalimidineacetic acid, with constant stirring, of 28.7 g thionyl chloride, and the solution is heated for about an hour on a water bath at 30-35° and toward the end at 40°. Gradual precipitation occurs of snow-white, small rhombic crystals. Complete precipitation is ensured by standing the reaction mixture for 3 hours; the crystals are then drained and washed with dry ether. Yield 12.77 g. The chloride melts at 123-124° (with decomp.); it is sparingly soluble in ether, benzene and xylene, readily soluble in acetic anhydride.

Found %: N 6.96, 6.97; Cl 16.35, 16.20. $C_{10}H_8O_3NCl$. Calculated %: N 6.68; Cl 16.94.

Phthalimidineacetic acid ureide. 2 g freshly prepared phthalimidineacetyl chloride is mixed with 1.8 g urea, put into 25 ml dry benzene and the mixture heated for 6 hours in a flask under a reflux condenser on a water bath. The precipitate is filtered, washed with ether and then with ammonia solution. Yield of unpurified product 2.14 g or about 96.4% of theory, calculated on the acid chloride. M.p. 222-223° (with decomp.). After one recrystallization from alcohol the m.p. rises to 229-230° (with decomp.). The product separates from alcohol as small, white, transparent prisms. Sparingly soluble in water, ethyl alcohol and dilute hydrochloric acid.

The preparation proved to be inactive in pharmacological tests.

Heating of the ureide with a large excess of conc. hydrochloric acid (sp. gr. 1.19) does not result in ring closure but only in hydrolysis of the ureide, and phthalimidineacetic acid is formed (m.p. 180-181°).

N-Acetylphthalimidineacetic acid. 1 g phthalimidineacetic acid is mixed with a large amount of acetic anhydride (25-30 g) and boiled for 4 hours. After cooling, the mass is diluted with double the amount of water. The 0.67 g of precipitate is recrystallized from alcohol to give long, transparent, small prisms, m.p. 186-188°.

Found %: N 6.05, 6.21. $C_{12}H_{11}O_4N$. Calculated %: N 6.00.

The ethyl ester. 2.75 g phthalimidineacetic acid and 7 g dry ethyl alcohol, saturated with hydrogen chloride, are heated for 4 hours on the water bath; the excess alcohol is then distilled off; to the residue is added triple the amount of water. The separated viscous, yellow-brown oil gradually solidifies. It is neutralized with sodium carbonate solution and the resultant white flocs are filtered off and washed with water. Yield of crude product 2.6 g or about 82.5% of theory, calculated on phthalimidineacetic acid. M.p. 115-116°, rising to 119-120° after recrystallization from ether (white, transparent platelets). Readily soluble in alcohol, poorly in water.

Found %: N 6.58, 6.62. $C_{12}H_{13}O_3N$. Calculated %: N 6.39.

Reaction of ethyl phthalimidineacetate with urea. 2 g of the ester and 0.6 g urea are heated for 3 hours in an alcoholic solution of sodium ethylate (0.23 g in 5 ml alcohol) on a water bath at 70°. 0.98 g substance with m.p. 215-218° was separated. After recrystallization from water the m.p. rose to 220-221°. The compound proved to be the amide of phthalimidineacetic acid and did not depress the melting point of a specially prepared sample (see below). In addition 0.3 g of a compound less easily soluble in water was isolated. When recrystallized from a large quantity of water, the ureide of phthalimidineacetic acid with m.p. 229-230° was isolated; it did not depress the m.p. of the ureide from another batch.

More prolonged heating of the ester with urea in an alcoholic solution of sodium ethylate (3 hours on the boiling water bath) yielded exclusively the amide of phthalimidineacetic acid.

Phthalimidineacetamide. A dry ammonia stream is passed into a mixture of 2 g phthalimidineacetyl chloride and 25 ml dry benzene for 3 hours with constant cooling with ice water. The precipitate is filtered after standing for 8-10 hours and washed with sodium carbonate solution and water. After drying, 1.46 g product with m.p. 217-218° is obtained in the form of needlets. After recrystallization from water the m.p. rose to 224-225°. Yield 1.05 g or 58% calculated on the chloride.

Found %: N 14.90, 14.83 . $C_{10}H_{10}O_2N_2$. Calculated %: N 14.74.

The highest yield of the amide is obtained by passing dry ammonia into a mixture of the acid chloride, dry toluene and xylene. In the same conditions as described above, 12 g acid chloride gave 7.8 g amide or about 71% of theory.

Methylamide of phthalimidineacetic acid. Prepared by reaction of the acid chloride with methylamine; melts at 183-185°; crystallizes in slender, white needlets; soluble in acids, alcohol and hot water; insoluble in caustic alkalies and ether.

Found %: N 13.82. $C_{11}H_{12}O_2N_2$. Calculated %: N 13.72.

2'-Carboxyphenyl-5-imidazolone (VII). Gradual addition is made at −5° to −7° of 5 g phthalimidineacetamide to a solution of 8.4 g bromine and 18.22 g potassium hydroxide in 90 ml water. The greater part of the amide dissolves. After the whole amount has been introduced, the reaction mass is heated for 30-40 minutes at 75-80°; it is then cooled externally with ice water and acidified with strong hydrochloric acid. A yellow precipitate (5.3 g) comes down; it is worked up with 10% sodium carbonate and filtered from the small quantity of residue insoluble in the soda. Acidification of the resultant alkaline solution with hydrochloric acid brings down 3.02 g of a mixture of two substances with the unsharp m.p. of 168-185°. Microscopic observation reveals transparent white platelets and clusters of needlets.

Two treatments with absolute alcohol and recrystallization from water of the alcohol-insoluble residue gave 0.6 g of a compound with m.p. 229-230° and the elementary composition $C_{10}H_{10}O_3N_2$.

On the basis of analyses and a study of the properties of this substance, the structure of carboxyphenylimidazolone could be assigned to it.

Found %: C 58.29, 58.13; H 4.37, 4.97; N 13.61, 13.62. $C_{10}H_{10}O_3N_2$. Calculated %: C 58.25; H 4.85; N 13.59. Determination of the acid equivalent: found 205.3; calculated 206.

During the melting point determination the substance melted at 229-230° with decomposition and vigorous gas evolution. The substance solidifying in the capillary melts at 161-162° when heated again. This melting point is characteristic of 5-phenylimidazolone (VIII). Consequently the substance undergoes decarboxylation when heated.

Decarboxylation can be most simply effected by heating with naphthalene. 0.18 g carboxy derivative is mixed with 10 times the amount of naphthalene and the mixture heated at the boiling point of naphthalene for 1½ - 2 hours. After cooling, the pulverized mass is treated 3 times with hydrochloric acid solution (1:1). The combined acid solutions are made alkaline with 15% sodium hydroxide solution and left to stand for 1½ - 2 hours while cooling externally with ice water. The precipitate is drained at the pump. After drying, the yield is 0.07 g. The product melts sharply at 160-161° after recrystallization from water and alcohol and does not depress the melting point of an authentic specimen of pure phenylimidazolone.

It was previously pointed out that 3.02 g of the mixture of substances separated from sodium carbonate solution was worked up with alcohol. The alcohol-soluble compound was isolated in the amount of 2.05 g and identified as phthalimidineacetic acid.

After removal of the carboxyphenylimidazolone, the acid filtrates contain mainly phthalimidineacetic acid which was isolated from the filtrates both as such and as the ethyl ester; for this purpose the filtrates were made alkaline with ammonia, evaporated to dryness and treated with absolute alcohol.

The Hofmann reaction was repeated several times with slight variations of temperature, alkali concentration and duration of reaction with alkali hypobromite. The yields of carboxyphenylimidazolone fluctuated fairly widely (13% when the amide was heated immediately after introducing it into hypobromite solution; 26% if the introduced amide was heated only after standing for 3 hours at room temperature).

In all cases two main products were isolated; carboxyphenylimidazolone and phthalimidineacetic acid.

SUMMARY

1. Phthalimidineacetic acid was characterized through the preparation of its acid chloride, ureide, amide, methylamide, ethyl ester and N-acetyl derivative.

2. A study was made of the condensation of the ethyl ester of phthalimidineacetic acid with urea in presence of sodium ethylate, and it was established that the reaction yielded the amide or a mixture of the ureide and the amide of phthalimidineacetic acid.

3. It was established that reaction of the amide of phthalimidineacetic acid with potassium hypobromite gives 2'-carboxyphenyl-5-imidazolone, which readily decarboxylates to the previously known 5-phenylimidazolone.

4. It is shown that the yield of carboxyphenylimidazolone depends in the main on the duration of the reaction of the amide with potassium hypobromite.

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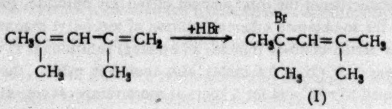
SYNTHESIS OF HYDROCARBONS

XXXVIII. SYNTHESIS OF ALKENES AND ALKANES WITH TWO QUATERNARY CARBON ATOMS

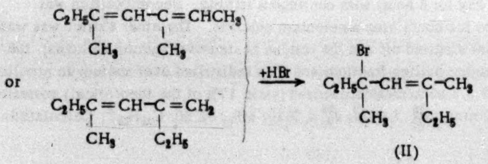
R. Ya. Levina, N. P. Shusherina, N. I. Volchinskaya and M. Yu. Lurye

Addition of hydrogen bromide to some conjugated alkadienes with an iso structure, for example to 2,4-dimethylpentadiene-1,3 and 3,5-dimethylheptadiene-2,4, leads to formation of tertiary bromides of the allyl type whose structure in each case excludes the possibility of formation of the isomeric bromide by allyl rearrangement:



$$CH_3\underset{CH_3}{C}=CH-\underset{CH_3}{C}=CH_2 \xrightarrow{+HBr} CH_3\overset{Br}{\underset{CH_3}{C}}-CH=\underset{CH_3}{C}-CH_3$$

(I)



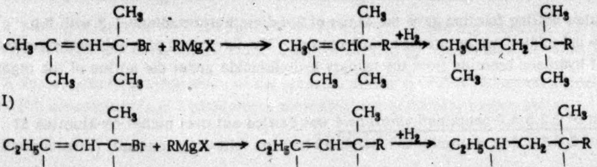
$$C_2H_5\underset{CH_3}{C}=CH-\underset{CH_3}{C}=CHCH_3$$

or

$$C_2H_5\underset{CH_3}{C}=CH-\underset{C_2H_5}{C}=CH_2 \xrightarrow{+HBr} C_2H_5\overset{Br}{\underset{CH_3}{C}}-CH=\underset{C_2H_5}{C}-CH_3$$

(II)

In our previous researches [1,2,3] it was established that the reaction between allylic bromides and primary or secondary alkyl magnesium halides is a method of synthesis of olefinic hydrocarbons, hydrogenation of which could yield paraffinic hydrocarbons containing one quaternary carbon atom:



$$CH_3-\underset{CH_3}{C}=CH-\overset{CH_3}{\underset{CH_3}{C}}-Br + RMgX \longrightarrow CH_3\underset{CH_3}{C}=CH\overset{CH_3}{\underset{CH_3}{C}}-R \xrightarrow{+H_2} CH_3\underset{CH_3}{CH}-CH_2-\overset{CH_3}{\underset{CH_3}{C}}-R$$

(I)

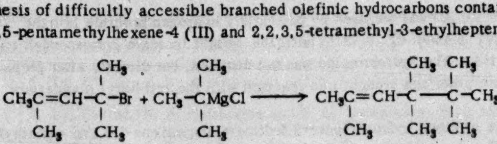
$$C_2H_5\underset{CH_3}{C}=CH-\overset{CH_3}{\underset{C_2H_5}{C}}-Br + RMgX \longrightarrow C_2H_5\underset{CH_3}{C}=CH-\overset{CH_3}{\underset{C_2H_5}{C}}-R \xrightarrow{+H_2} C_2H_5\underset{CH_3}{CH}-CH_2-\overset{CH_3}{\underset{C_2H_5}{C}}-R$$

(II)

where R = CH_3, C_2H_5, C_3H_7, C_4H_9, iso-C_3H_7, iso-C_4H_9 and iso-C_5H_{11}

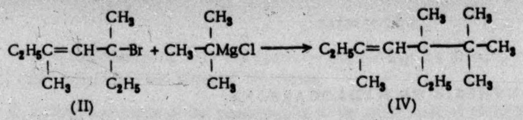
The structure of the so-synthesized hydrocarbons was confirmed by the methods of oxidation or ozonization and Raman spectrography [1,3].

In the present investigation, these tertiary allylic bromides (I and II) (2,4-dimethylpentadiene-1,3 hydrobromide and 3,5-dimethylheptadiene-2,4 hydrobromide) were brought into reaction with an organomagnesium compound containing a tertiary alkyl group (tert-butyl magnesium chloride); this reaction served as a method of synthesis of difficultly accessible branched olefinic hydrocarbons containing two quaternary carbon atoms: 2,2,3,3,5-pentamethylhexene-4 (III) and 2,2,3,5-tetramethyl-3-ethylheptene-4 (IV)



$$CH_3\underset{CH_3}{C}=CH-\overset{CH_3}{\underset{CH_3}{C}}-Br + CH_3-\overset{CH_3}{\underset{CH_3}{C}}MgCl \longrightarrow CH_3\underset{CH_3}{C}=CH-\overset{CH_3}{\underset{CH_3}{C}}-\overset{CH_3}{\underset{CH_3}{C}}-CH_3$$

(I) (III)



$$\underset{CH_3}{C_2H_5C}{=}CH{-}\underset{C_2H_5}{\overset{CH_3}{C}}{-}Br + CH_3{-}\underset{CH_3}{\overset{CH_3}{C}}MgCl \longrightarrow \underset{CH_3}{C_2H_5C}{=}CH{-}\underset{C_2H_5}{\overset{CH_3}{C}}{-}\underset{CH_3}{\overset{CH_3}{C}}{-}CH_3$$

(II) (IV)

Catalytic hydrogenation of the synthesized alkenes yielded the corresponding alkanes: 2,2,3,3,5-pentamethylhexane and 2,2,3,5-tetramethyl-3-ethylheptane.

EXPERIMENTAL

2,2,3,3,5-Pentamethylhexene-4 and 2,2,3,3,5-pentamethylhexane. Tert-butyl chloride was prepared by addition of hydrogen chloride to isobutene in the gas phase [4].

An ethereal solution (1:1) of 70 g (0.75 mole) tert-butyl chloride was slowly added with heating (at the rate of not more than one drop per second) to 18 g magnesium covered with a layer of absolute ether and previously activated with 1.5 ml ethylene bromide. After introduction of the total amount of tertiary chloride, the reaction mixture was heated with stirring for two hours. To the so-obtained ethereal solution of tert-butyl magnesium chloride, cooled to −40°, was added dropwise over a period of 30-40 minutes an ethereal solution (1:1) of the freshly prepared hydrobromide of 2,4-dimethylpentadiene-1,3* (72 g, 0.5 mole), also cooled to −30°. The reaction mixture was then stirred for 3 hours while being cooled to −30° and for 2 hours at room temperature, allowed to stand overnight, and heated on the following day for 8 hours with continuous stirring. Decomposition was effected by pouring the reaction mixture on to ice containing ammonium chloride. The ether extract was washed and dried with calcium chloride, the ether was distilled off and the residue heated over sodium (6 hours); the obtained hydrocarbon was distilled off from higher boiling fractions and then redistilled over sodium in a column with 40 theoretical plates. The isolated 2,2,3,3,5-pentamethylhexene-4 (yield 17% of the theoretical) possessed the following constants: b.p. 170-170.2° (760 mm); n_D^{20} 1.4470; d_4^{20} 0.7836; MR_D 52.60. $C_{11}H_{22}F$. Calculated: MR_D 52.53.

7.530 mg substance: 23.660 mg CO_2; 9.590 mg H_2O. 6.310 mg substance: 19.850 mg CO_2; 8.030 mg H_2O. Found %: C 85.75, 85.85. H 14.25, 14.24. $C_{11}H_{22}$. Calculated %: C 85.60; H 14.40.

2,2,3,3,5-Pentamethylhexene-4 has not been described in the literature.

Fractionation of the higher boiling fraction gave the dimer of 2,4-dimethylpentadiene-1,3 with b.p. 217-218° at 760 mm (yield 17% calculated on the initial hydrobromide). The formation of 2,4-dimethylpentadiene-1,3 is explained by cleavage of hydrogen bromide from the tertiary hydrobromide under the action of the organomagnesium compound.

Catalytic hydrogenation of 2,2,3,3,5-pentamethylhexene-4 was carried out over nickel-on-alumina at 160-170° and led to formation of 2,2,3,3,5-pentamethylhexane which had the following constants (after redistillation in a column (over sodium):

B.p. 172.8-173.5 (760 mm); n_D^{20} 1.4302; d_4^{20} 0.7673; MR_D 52.88; calculated 52.99.

2,2,3,3,5-Pentamethylhexane has not been described in the literature.

2,2,3,5-Tetramethyl-3-ethylpentene-4 and 2,2,3,5-tetramethyl-3-ethylheptane. The preparation of the hydrobromide of 3,5-dimethylheptadiene-2,4** and its reaction with tert-butyl magnesium chloride was carried out by the above-described procedure (for the hydrobromide of 2,4-dimethylpentadiene-1,3). After working up the reaction product in the usual manner and distilling off the ether, the residue was fractionally distilled over sodium. Two fractions were obtained:

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* The hydrobromide of 2,4-dimethylpentadiene-1,3 [2] was prepared by passing dry hydrogen bromide into the cooled dienic hydrocarbon (b.p. 93-94° at 755 mm; n_D^{20} 1.4448; d_4^{20} 0.7376) until the weight increase corresponded to that required for the addition of one molecule of HBr. The hydrobromide was not distilled, but directly after preparation it was dissolved in an equal volume of absolute ether and brought into reaction with the tert-butyl magnesium chloride.

** Hydrogenation was performed on a mixture of diene hydrocarbons −3,5-dimethylheptadiene-2,4 and 4-methyl-2-ethylhexadiene-1,3 −whose components differed only in the position of the double bond: b.p. 136-142° (760 mm); n_D^{20} 1.4495; d_4^{20} 0.7675 [3].

1) b.p. 130-136°; n_D^{20} 1.4260; 2) b.p. 200-211°.

Distillation of the second fraction in a column with 40 theoretical plates gave a 14% yield of 2,2,3,5-tetramethyl-3-ethylheptene-4:

B.p. 210.5-211.5° (755 mm); n_D^{20} 1.4574; d_4^{20} 0.8012; MR_D 61.91. $C_{13}H_{26}F$. Calculated: MR_D 61.76.

5.792 mg substance: 18.150 mg CO_2; 7.490 mg H_2O. 6.340 mg substance: 19.905 mg CO_2; 8.220 mg H_2O. Found %: C 85.52, 85.68; H 14.47, 14.51. $C_{13}H_{26}$. Calculated %: C 85.72; H 14.28.

2,2,3,5-Tetramethyl-3-ethylpentene-4 is not described in the literature.

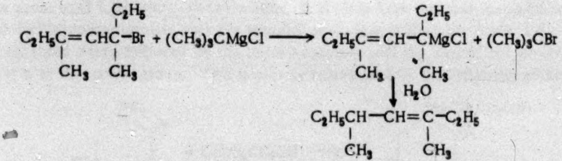
Distillation of the lower boiling fraction (b.p. 130-136°) in a column with 40 theoretical plates gave a hydrocarbon (yield 55% of the theoretical calculated on the initial hydrobromide) with the following constants:

B.p. 130.5-131° (750 mm); n_D^{20} 1.4222; d_4^{20} 0.7353; MR_D 43.54. $C_9H_{18}F$. Calculated: MR_D 43.29.

The constants indicate that the hydrocarbon is 3,5-dimethylheptene-3.

Literature data for 3,5-dimethylheptene-3 [5]: b.p. 130.5-130.6° (749 mm); n_D^{20} 1.4218; d_4^{20} 0.7350.

The formation of 3,5-dimethylheptene-3 by reaction of tert-butyl magnesium chloride with the hydrobromide of 3,5-dimethylheptadiene-2,4 may be explained by the following secondary reaction:



$$C_2H_5\underset{CH_3}{C}=CH\underset{CH_3}{\overset{C_2H_5}{C}}-Br + (CH_3)_3CMgCl \longrightarrow C_2H_5\underset{CH_3}{C}=CH-\underset{CH_3}{\overset{C_2H_5}{C}}MgCl + (CH_3)_3CBr \xrightarrow{H_2O} C_2H_5\underset{CH_3}{CH}-CH=\underset{CH_3}{C}-C_2H_5$$

Catalytic hydrogenation of 2,2,3,5-tetramethyl-3-ethylheptene-4 over nickel-on-alumina at 160-170° led to formation of 2,2,3,5-tetramethyl-3-ethylheptane with the following constants (after distillation in a column): b.p. 214.5-215° (760 mm); n_D^{20} 1.4440; d_4^{20} 0.7891; MR_D 61.83, calculated 62.23.

5.740 mg substance: 17.780 mg CO_2; 7.890 mg H_2O. 7.130 mg substance: 22.140 mg CO_2; 9.710 mg H_2O. Found %: C 84.53, 84.73; H 15.38, 15.24. $C_{13}H_{28}$. Calculated %: C 84.80; H 15.28.

A Raman spectrographic study of the prepared alkane revealed frequencies, according to the data of Stepanov [6], characteristic of hydrocarbons possessing two quaternary carbon atoms.

SUMMARY

1. Our previously developed method of synthesis of hydrocarbons containing a quaternary carbon atom was applied to the reaction of the hydrobromides of 2,4 dimethylpentadiene-1,3 and 3,5-dimethylheptadiene-2,4 with organomagnesium compounds to give previously undescribed hydrocarbons with two quaternary carbon atoms –2,2,3,3,5-pentamethylhexene-4 and 2,2,3,5-tetramethyl-3-ethylheptene-4.

2. Hydrogenation of these hydrocarbons yielded the difficultly accessible alkanes, 2,2,3,3,5-pentamethylhexane and 2,2,3,5-tetramethyl-3-ethylheptane, not previously described in the literature.

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* See Consultants Bureau translation, p. 903.

** See Consultants Bureau translation, p. 641.

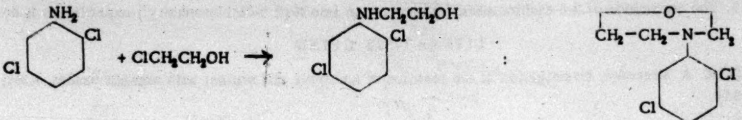
THE PROBLEM OF THE REACTION OF α-HALOHYDRINS WITH AMINES

K. D. Petrov and E. S. Lagucheva

Krasusky [1] stated that "the formation of α-amino alcohols from α-monochlorohydrins proceeds through α-oxides" which are intermediate products in the course of reaction of ammonia and amines with α-monochlorohydrins.

As we know, the foregoing observation of Krasusky and his rule for the order of addition of ammonia and amines to asymmetrical oxides is utilized for determination of the structure of amino alcohols prepared by reaction of α-halohydrins with ammonia and amines. But Krasusky also suggested the possibility of direct substitution of the halo compound at an amino group in the reactions of α-halohydrins with amines. However, he did not produce an example of this.

In this connection it appeared of interest to consider the reaction of ethylene chlorohydrin with 2,5-dichlorophenylamine (I). This reaction proceeds smoothly with heating in presence of water (procedure of Shorygin [2,3]), with formation for the most part of 2,5-dichlorophenylethanolamine (II) (2,5-dichlorophenyl-β-hydroxyethyl amine). But, as was found, in the same conditions the corresponding chlorohydrin of ethylene oxide does not react with 2,5-dichlorophenylamine. It is clear from this that the reaction of ethylene chlorohydrin with 2,5-dichlorophenylamine does not proceed according to Krasusky's rule, i.e., not through the stage of formation of ethylene oxide followed by the latter's reaction with the amine, but involves direct substitution of the chlorohydrin at the amino group. This is clearly represented by the following scheme:



(I) (II) (III)

Formation of 2,5-dichlorophenylethanolamine is confirmed by analysis for the nitrogen content and by transformation into N-(2,5-dichlorophenyl)-oxazolidine (III)

EXPERIMENTAL

2,5-Dichlorophenylethanolamine (2,5-dichlorophenyl-β-hydroxyethylamine) was prepared by reaction of 486 g (3 moles) of 2,5-dichlorophenylamine with 362.2 g (4.5 moles) ethylene chlorohydrin in presence of 43.5 ml water. The reaction was performed in a three-necked flask fitted with reflux condenser for a period of 19 hours with uninterrupted mechanical stirring. During the reaction the temperature was held within the range of 130-135°. At the end of the reaction the water and excess ethylene chlorohydrin were distilled off in the vacuum of a water jet pump. The residue was neutralized with saturated soda solution (159 g Na_2CO_3). The product was extracted with ether, separated from the water layer, dried with potassium carbonate, filtered, and fractionated. Ether was first distilled off on the water bath, and then the product was fractionated in vacuum. The first fraction was unreacted 2,5-dichlorodiphenylamine (128 g came over up to 130° at 3 mm). The next fraction was 41 g at 130-163° (3 mm). Then the 2,5-dichlorophenylethanolamine (256 g) came over at 163-165° (3 mm). The viscous still residue weighed 73 g.

2,5-Dichlorophenylethanolamine solidified in the receiver to a dense crystalline white mass contaminated by a yellowish oil. Its yield was 56.20%, calculated on the reacted 2,5-dichlorophenylamine. The 2,5-dichlorophenylethanolamine was purified by recrystallization from aqueous alcohol, from which it came down as white needles with m.p. 53-54°.

1.2310 g substance: 11.10 ml 0.5 N H_2SO_4. 1.1063 g substance: 10.00 ml 0.5 N H_2SO_4. Found %: N 6.32, 6.33. $C_8H_9ONCl_2$. Calculated %: N 6.79.

We also attempted to prepare 2,5-dichlorophenylethanolamine by passing ethylene oxide into 2,5-dichlorophenylamine heated to 100-150°, but this method failed. This reaction is not catalyzed by water, alcohol or hydrochloric acid taken in small quantity.

N-(2,5-Dichlorophenyl)-oxazolidine. Into a flask fitted with a stirrer and reflux condenser was introduced 41.2 g (0.2 mole) 2,5-dichlorophenylethanolamine dissolved in 30 ml alcohol. To the solution was gradually added from a dropping funnel 32.4 g 37% formaldehyde (0.4 mole CH_2O). The reaction was conducted with constant stirring and was accompanied by evolution of heat. After the whole amount of formaldehyde had been added, the stirring of the reaction mass was continued for a further 30 minutes. At the conclusion of the reaction the alcohol was distilled off from the reaction product in a low vacuum. The N-(2,5-dichlorophenyl)oxazolidine was then separated from the aqueous layer and subjected to vacuum fractionation. The N-(2,5-dichlorophenyl)-oxazolidine fraction was collected at 137-139° (4 mm). Yield 28.03 g (64.30% of the theoretical). The distilled product was a light-yellow oil.

d_{20}^{20} 1.3709; n_D^{20} 1.5956; MR_D 54.08; calculated 53.36.

0.9045 g substance: 40.2 ml 0.1 N H_2SO_4. 1.5848 g substance: 69.0 ml 0.1 N H_2SO_4. Found %: N 6.21, 6.09. $C_9H_9ONCl_2$. Calculated %: N 6.42.

SUMMARY

1. It was established that the formation of 2,5-dichlorophenylethanolamine from ethylene chlorohydrin and 2,5-dichlorophenylamine does not proceed according to Krasusky's mechanism, i.e., through the stage of formation of ethylene oxide and reaction of the latter with the amine, but through direct substitution of the halo compound at the amino group.

2. The conversion of 2,5-dichlorophenylethanolamine into N-(2,5-dichlorophenyl)-oxazolidine is described.

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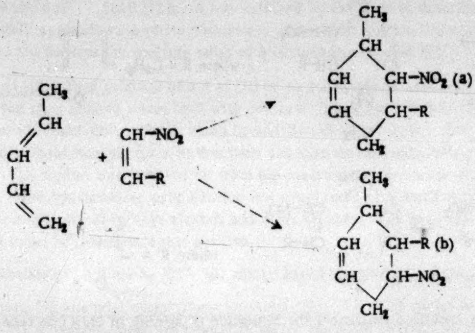
REACTION OF PIPERYLENE AND 2,4-HEXADIENE WITH UNSATURATED NITRO COMPOUNDS

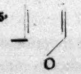
E. G. Kataev and P. S. Matveeva

In continuation of the study of the reactions of the diene synthesis with piperylene and 2,4-hexadiene undertaken some years ago [1,2], we have condensed piperylene with nitroamylene, nitrostyrene, and furylnitroethylene, and 2,4-hexadiene with nitrostyrene and furylnitroethylene. The possibility of utilizing α,β-unsaturated nitro compounds in the diene synthesis with acyclic dienes had been demonstrated as far back as 1938 in the reactions of butadiene, isoprene and 2,3-dimethylbutadiene with nitroamylene and nitrostyrene [3-5]. Up to now, however, the question of orientation in the reactions of nitrodienophiles with unsymmetrical dienes has not been discussed in the literature. We considered it to be a matter of interest to fill this gap by a detailed examination of the reaction of nitroamylene and nitrostyrene with piperylene and on the basis of the evidence of the structure of the resultant adducts to show the order of addition. A further objective of the study of the reactions of nitrostyrene and furylnitroethylene (application of the latter as a dienophile is here described for the first time) with piperylene, hexadiene and butadiene (the latter condensed with furylnitroethylene) was the widening of the field of synthesis of hydroaromatic nitro compounds with the help of the diene reaction.

The formation of two isomeric adducts may be expected to result from reaction of nitrostyrene, nitroamylene and furylnitroethylene with piperylene:



where R = $-CH_2-CH_2-CH_3$, $-C_6H_5$,



On the basis, however, of electronic considerations which indicated possible polarization of our selected reactants (considerations expounded in one of our earlier communications [1]), we were inclined to expect the formation of only adduct (a). Experiment actually confirmed our ideas.

Heating of piperylene with nitroamylene, nitrostyrene and furylnitroethylene in sealed tubes without a solvent at 150° for 8-15 hours gave, respectively, 2-methyl-6-n-propyl-1-nitro-Δ^3-cyclohexene, 2-methyl-6-phenyl-1-nitro-Δ^3-cyclohexene, and 2-methyl-6-α-furyl-1-nitro-Δ^3-cyclohexene.

Evidence for the structure of the adducts was obtained by selenium dehydrogenation at 320-350° for 20 hours followed by oxidation of the dehydrogenation products to aromatic acids in accordance with the schemes:*

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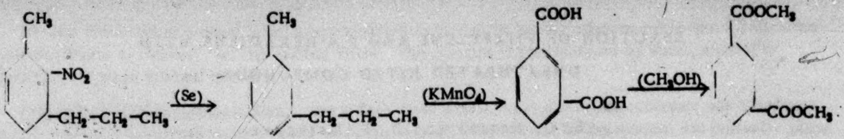
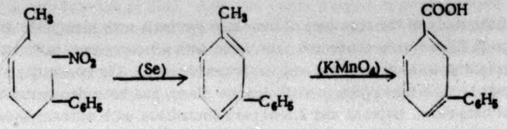
* The structure of the piperylene-furylnitroethylene adduct, due to its high resinifying tendency, was not demonstrated but was inferred by analogy with the other adducts.



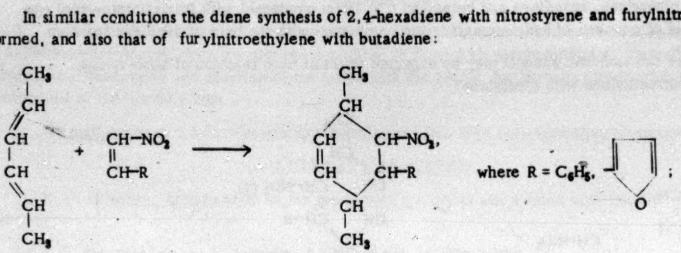
CH₃
NO₂
CH₂–CH₂–CH₃
(Se)
CH₃
CH₂–CH₂–CH₃
(KMnO₄)
COOH
COOH
(CH₃OH)
COOCH₃
COOCH₃



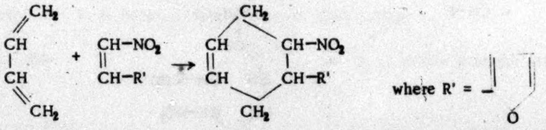
CH₃
NO₂
C₆H₅
(Se)
CH₃
C₆H₅
(KMnO₄)
COOH
C₆H₅

When the adducts are heated with selenium at a temperature at which dehydrogenation does not yet take place (270-280°), evolution of oxides of nitrogen and water was observed, which is consistent with our previous observations [1] that functional groups of the type of CN, CHO, COOH and COOR, attached to a hydroaromatic ring, are eliminated in course of dehydrogenation.

In similar conditions the diene synthesis of 2,4-hexadiene with nitrostyrene and furylnitroethylene was performed, and also that of furylnitroethylene with butadiene:



CH₃
CH
CH
CH
CH
CH₃
+
CH–NO₂
CH–R
CH₃
CH
CH
CH
CH–NO₂,
CH–R
CH
CH₃
where R = C₆H₅,
O
;



CH₂
CH
CH
CH₂
+
CH–NO₂
CH–R'
CH₂
CH
CH
CH–NO₂
CH–R'
CH₂
where R' =
O

In view of the fact that in the specified conditions the formation is possible of only one type of adduct, their structure was not considered.

All the synthesized hydroaromatic nitro compounds (with exception of the adduct of piperylene with nitrostyrene, m.p. 80-82°) are oily liquids which seriously irritate the mucous membranes of the nose and eyes.

In the case of adducts of piperylene hexadiene and with nitrostyrene, the possibility was examined of their reduction to the corresponding amines with the help of iron filings in an acetic acid medium. 2-Methyl-6-phenyl-Δ^3-cyclohexenylamine (m.p. of hydrochloride 268-270°) and 2,5-dimethyl-6-phenyl-Δ^3-cyclohexenylamine (m.p. of hydrochloride 290-292°) were prepared and characterized in the form of their hydrochlorides.

The constants of the prepared compounds are listed in the table.

EXPERIMENTAL

1. 2-Methyl-6-n-propyl-1-nitro-Δ^3-cyclohexene (I). 7 g (0.06 mole) of 1-nitroamylene-1 [8], 7.2 g (0.18 mole) of piperylene, and 0.1 g of hydroquinone were heated in sealed tubes for 15 hours at 150°. After distilling off the excess of diene, the residue was vacuum-fractionated from an Arbuzov flask to give 11 g of (I) (70%) in the form of a yellow oil with a strong odor which irritated the mucous membranes.

B.p. 108-110° at 6 mm; d_4^{20} 1.0030; n_D^{20} 1.4728; MR_D 51.19; calculated 51.40.

0.0922 g substance: 6.4 ml N_2 (22°, 753 mm). Found %: N 7.90. $C_{10}H_{17}O_2N$. Calculated %: N 7.65.

Determination of the structure of (I). 2 g of (I) was heated with 10 g selenium black in a sealed tube for 6-7 hours at 280°. When the tube was opened the odor of nitrogen oxides was detected and water droplets had condensed on the sides. The tube was again sealed and heated for another 20 hours at 320-350°. The tube was opened (H_2Se was evolved), the contents extracted with ether, the ether solution filtered, and the residue distilled in vacuum from an Arbuzov flask. The condensate was an oily liquid with b.p. 78-80° at 10 mm; n_D^{20} 1.5030 (close to the constants of m-propyltoluene: b.p. 181.5-182.5°; n_D^{20} 1.4951 [9]); it was oxidized with aqueous potassium permanganate solution with heating on the water bath and vigorous shaking for 20 hours. At the end of the oxidation the manganese dioxide was repeatedly washed with boiling water, the wash liquors were combined with the main filtrate and the whole evaporated on the water bath to a small volume. After acidification with dilute hydrochloric acid (1:2) the white precipitate was recrystallized from water. The m.p. of the substance and of a mixed specimen with isophthalic acid was 345-347°. The prepared acid was esterified to the dimethyl ester (using $CH_3OH + HCl$). The m.p. of the ester and that of its mixture with dimethyl-m-phthalate was 67-68° (recrystallized from dilute alcohol) [6].

2. 2-Methyl-6-phenyl-1-nitro-Δ^3-cyclohexene (II). 5 g (0.03 mole) β-nitrostyrene [10], 7 g (0.09 mole) piperylene and 0.1 g hydroquinone were heated in sealed tubes for 15 hours at 150°. After opening the tubes and distilling off the excess of piperylene, the residue solidified. Recrystallization from alcohol gave 6 g (87%) of (II) in the form of long, white needles, m.p. 80-82°.

0.1735 g substance: 9.7 ml N_2 (19.5°, 758 mm). Found %: N 6.41. $C_{13}H_{15}O_2N$. Calculated %: N 6.51.

Evidence of structure of (II). 2 g of (II) was heated with a fivefold excess of selenium in a sealed tube for 20 hours at 320-350°. At the conclusion of dehydrogenation the contents of the tube were extracted with ether, the solution filtered, the ether driven off and the residue fractionated in vacuum from an Arbuzov flask. The distillate was a viscous oil with b.p. 147-150° at 20 mm, n_D^{20} 1.5900 (close to the constants of 3-methyldiphenyl: b.p. 148-150° at 20 mm; n_D^{20} 1.5916 [11]). It was oxidized by the method described above. Acidification of the concentrated filtrate brought down a white precipitate which after recrystallization from dilute alcohol melted at 161-162° and did not depress the melting point of 3-phenylbenzoic acid [7].

Reduction of (II). To a solution of 4 g of (II) in 30 g 80% acetic acid was added 15 g fine iron filings, and the whole heated on a boiling water bath with constant stirring for 8 hours. The reaction mixture solidified to a slurry which was brought into solution again by addition of 50 ml water. For completion of the reaction, the mixture was stirred without heating for a further hour and then treated with 30% sodium hydroxide solution until strongly alkaline. The amine was distilled off from the reaction mixture with steam and collected in dilute hydrochloric acid (1:2). The hydrochloric acid solution was evaporated to a small volume and the white precipitate recrystallized from a mixture of methyl alcohol and butyl acetate. The beautiful silvery needlets of the hydrochloride melted at 268-270°. Beilstein test positive.

0.1015 g substance: 5.6 ml N_2 (21°, 761 mm). Found %: N 6.39. $C_{13}H_{18}NCl$. Calculated %: N 6.28.

3. 2,5-Dimethyl-6-phenyl-1-nitro-Δ^3-cyclohexene (III). 5 g (0.03 mole) β-nitrostyrene, 8.5 g (0.09 mole) 2,4-hexadiene and 0.1 g hydroquinone are heated in sealed tubes for 16 hours at 150-155°. After distilling off the excess of hexadiene, the residue is fractionated in vacuum to give 6.36 g of (III) (82.6% in the form of a thick, yellow oil, strongly irritating the mucous membranes, b.p. 149-151° at 4 mm; d_4^{20} 1.1050; n_D^{20} 1.5422; MR_D 65.82; calculated 65.87.

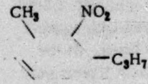
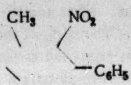
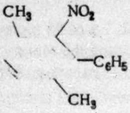
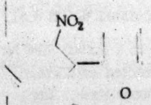
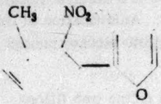
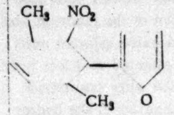
0.0404 g substance: 2.3 ml N_2 (23°, 760 mm). Found %: N 6.54. $C_{14}H_{17}O_2N$. Calculated %: N 6.60.

Reduction of (III) was performed in exactly the same manner as that of (II). There was obtained the hydrochloride of 2,5-dimethyl-6-phenyl-Δ^3-cyclohexenylamine in the form of a white, finely crystalline powder with m.p. 290-292° (from alcohol).

0.1017 g substance: 6.3 ml N_2 (19°, 747 mm). Found %: N 7.15. $C_{14}H_{20}NCl$. Calculated %: N 6.96.

4. 1-Nitro-6-(α)-furyl-Δ^3-cyclohexene (IV). 5 g (0.03 mole) furylnitroethylene [12], 6 g (0.09 mole) butadiene and 0.1 g hydroquinone were heated in sealed tubes for 10 hours at 150°. Considerable resinification was observed. After driving off the excess of butadiene the residue was fractionated to give 3.18 g (45.6%) of (IV) in the form of a yellow oil which very quickly darkened in the air and strongly irritated the mucous membranes: b.p. 148-150° at 200 mm; d_4^{20} 1.1970; n_D^{20} 1.5350; MR_D 50.21; calculated 49.91.

0.1956 g substance: 12.4 ml N_2 (22°, 753 mm). Found %: N 7.27. $C_{10}H_{11}O_3N$. Calculated %: N 7.25.

Prep. No.	Adduct	Reaction conditions (diene: dienophile)	B.p.	n_D^{20}	d_4^{20}	MR_D		Yield (%)
						found	calculated	
I		Without solvent, 150° 15 hours (3:1)	108-110° at 6 mm	1.4728	1.0030	51.19	51.40	70
II		Without solvent, 150° 10 hours (3:1)	M.p. 80-82°	–	–	–	–	87
III		Without solvent, 155° 16 hours (3:1)	149-151 at 4 mm	1.5422	1.1050	65.82	65.87	82.6
IV		Without solvent, 150° 10 hours (3:1)	148-150 at 200 mm	1.5350	1.1970	50.21	49.91	45.6
V		Without solvent, 150° 8 hours (3:1)	120-122 at 4 mm	1.5150	1.1550	54.30	54.53	55
VI		Without solvent, 150° 16 hours (3:1)	125-127 at 4 mm	1.5191	1.1411	59.08	59.15	45.6

5. 2-Methyl-6-(*a*)-furyl-1-nitro-Δ^3-cyclohexene (V). 5 g (0.03 mole) furylnitroethylene, 7.2 g (0.09 mole) piperylene and 0.1 g hydroquinone were heated in sealed tubes for 8 hours at 150°. Fractionation gave 4 g (55%) of (V) in the form of a light-yellow oil, rapidly oxidizing in the air; b.p. 120-122° at 4 mm; d_4^{20} 1.1550; n_D^{20} 1.5150; MR_D 54.30; calculated 54.53.

0.0743 g substance: 5.4 ml N_2 (21°, 752 mm). Found %: N 6.73. $C_{11}H_{13}O_3N$. Calculated %: N 6.49.

6. 2,5-Dimethyl-6-(*a*)-furyl-1-nitro-Δ^3-cyclohexene (VI). 5 g (0.03 mole) furylnitroethylene, 9 g (0.09 mole) 2,4-hexadiene and 0.1 g hydroquinone were heated in sealed tubes for 16 hours at 150°. Vacuum fractionation yielded 3.6 g (45.6%) of (VI) in the form of a yellow oil which quickly darkened in the air; b.p. 125-127° at 4 mm; d_4^{20} 1.1411; n_D^{20} 1.5191; MR_D 59.08; calculated 59.15.

0.0836 g substance: 4.7 ml N_2 (20°, 752 mm). Found %: N 6.50. $C_{12}H_{15}O_3N$. Calculated %: N 6.30.

SUMMARY

1. Reactions were carried out on the diene synthesis of piperylene with nitroamylene, nitrostyrene, and furylnitroethylene, and of butadiene with furylnitroethylene, and 6 new cyclohexene derivatives are described.

2. For the first time furylnitroethylene has been used as a dienophile.

3. By demonstrating the structure of the adducts of piperylene with nitroamylene and nitrostyrene, it was shown that the order of addition of these dienophiles to piperylene is in good accord with the direction of polarization of piperylene and the dienophile.

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* See Consultants Bureau translation, p. 73.

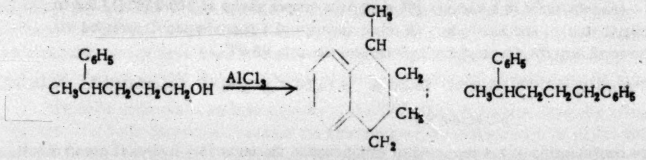
** See Consultants Bureau translation, p. 971.

ALKYLATION OF AROMATIC COMPOUNDS WITH ALCOHOLS

XVI. CONDENSATION OF 1,4-PENTANEDIOL WITH BENZENE

I. P. Tsukervanik and N. I. Bogdanova

Studies in our laboratory of the reactions of alkylation of aromatic compounds with difunctional reactants have shown the possibility of utilization of the greater activity of the secondary hydroxyl group of 1,3-butanediol. This enabled us to realize the hydroxyalkylation of a series of aromatic compounds [1]. In the further development of this investigation we have undertaken a study of the condensation of 1,4-pentanediol with benzene. In this case we may expect the formation of 4-phenylpentan-1-ol (I) which must readily cyclize to 1-methyltetrahydronaphthalene (II)



(I) (II) (III)

Since such a cycloalkylation is always observed in similar cases, the formation in the second stage of the condensations of 1,4-diphenylpentane (III) is less probable.

We performed a series of condensations of 1,4-pentanediol with benzene in presence of $AlCl_3$. In accordance with the mechanism of these condensations [2] it is necessary to use not less than 2 moles of $AlCl_3$ per mole of diol. By suitable choice of reaction conditions we showed the possibility of preparation of products (I) and (II) with a preponderance of one of these. 4-Phenylpentan-1-ol (I) is obtained in about 63% yield by operating with highly dilute benzene at room temperature; this was accompanied by 1-methyltetrahydronaphthalene (II) in 15% yield. When operating at higher temperatures (65-85°) the main product is (II) (50% of theory), while alcohol (I) is obtained in only 16% yield. Direct experiment showed that when 4-phenylpentanol was heated (75-85°) in benzene with $AlCl_3$, a high yield of 1-methyltetrahydronaphthalene is obtained. We were unable to find 1,4-diphenylpentane in a number of the products of alkylation, although small amounts of higher boiling fractions were isolated.

EXPERIMENTAL

1,4-Pentanediol was prepared by reduction of acetopropyl alcohol with sodium amalgam [3]. Yield 70% of the theoretical. B.p. 218-220°.

1. Reactants: 1,4-pentanediol 7.3 g (0.07 mole), benzene 150 ml, $AlCl_3$ 21 g (0.16 mole). The $AlCl_3$ was introduced in small portions, over a period of an hour, into the benzene-diol mixture with constant stirring. The mixture was held at 35-40° for 9 hours and then at 20-21° for 15 hours. After decomposition with water, the benzene layer was separated, dried and fractionated. There were obtained: 1-methyltetrahydronaphthalene 1.5 g (15% of theory), b.p. 105-110° at 18 mm; 4-phenylpentan-1-ol 7.2 g (62.5% of theory), b.p. 140-147° at 18 mm.

2. Reactants: 1,4-pentanediol 10.4 g (0.1 mole), benzene 100 ml, $AlCl_3$ 27 g (0.2 mole). After slow introduction of $AlCl_3$, the mixture was heated for 4 hours on the water bath at 75-85° and the products were: 1-methyltetrahydronaphthalene 7.6 g (52% of theory) and 4-phenylpentan-1-ol 2.6 g (16% of theory).

3. Reactants: 4-phenylpentan-1-ol 18.1 g (0.11 mole), benzene 50 ml, $AlCl_3$ 15.7 g (0.12 mole). After introduction of the $AlCl_3$ the mixture was heated for 4 hours at 75-85°. 1-Methyltetrahydronaphthalene with b.p. 105-107° at 18 mm was obtained. Yield 5 g (69% of theory).

The products of several condensations were subjected to repeated fractionation.

1-Methyltetrahydronaphthalene [4]—b.p. 88-89° (10 mm); n_D^{20} 1.5310; d_4^{25} 0.9539.

0.0982, 0.1322 g substance: 0.3238, 0.4367 g CO_2; 0.0844, 0.1143 g H_2O. Found %: C 89.98, 90.16; H 9.62, 9.67. $C_{11}H_{14}$. Calculated %: C 90.35; H 9.64.

Oxidation with nitric acid (sp.gr. 1.15) in sealed tubes at 130-150° gave phthalic acid with m.p. 188-189°. 1-Methylnaphthalene [5] was prepared by heating 1-methyl tetrahydronaphthalene with sulfur at 180-200° for 7 hours [6]. B.p. 108-109° (10 mm); n_D^{20} 1.6165; d_4^{20} 1.0192.

Picrate: m.p. 138° [7].

The same results were got in dehydrogenation of the product of experiment 3.

4-Phenylpentan-1-ol [8]. An oily liquid with a pleasant odor, b.p. 127-128° (8 mm); n_D^{20} 1.5170; d_4^{20} 0.9815.

Found %: C 80.24; H 9.85. $C_{11}H_{16}O$. Calculated %:: C 80.46; H 9.85.

Passage of the vapor of 4-phenylbutanol in a vacuum (30 mm) over copper gauze at 240-260° [1] led to formation of a mixture of the initial alcohol and aldehyde. A small quantity of 4-phenylbutanol, isolated via the bisulfite compound, was converted into the dinitrophenylhydrazone with m.p. 96-97°.

4.92 mg substance: 0.775 ml N_2 (30°, 721.5 mm). Found %: N 16.60. $C_{17}H_{18}O_4N_4$. Calculated %: N 16.36.

SUMMARY

1. It is shown that in the condensation of 1,4-pentanediol with benzene the secondary hydroxyl group reacts in the first instance. The resultant 4-phenylpentan-1-ol cyclizes to 1-methyltetrahydronaphthalene on heating with excess of $AlCl_3$.

2. By conducting the condensation under selected conditions, it can be directed in one direction or the other as desired.

3. The described condensations may serve as a preparative method of synthesis of 4-phenylpentan-1-ol (63% of theory) and of 1-methyltetrahydronaphthalene (52% of theory).

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* See Consultants Bureau translation, p. 891.

CHARACTERISTICS OF THE BROMINATION OF PHENYLTRICHLOROSILANE

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From the extremely small number of publications in the field of halogenation of aromatic silanes, we know that the action of halogens on aromatic organosilicon compounds may proceed in two directions. Thus the action of bromine on tetraphenylsilane [1] is accompanied not by bromination but by cleavage of the phenyl group. A similar reaction has been observed when bromine acts on p-bistriethylphenylsilane in presence of iron [2]. On the other hand, the action of chlorine on triethylphenylsilane led to triethylchlorophenylsilane [3]. Similarly, the action of chlorine on diphenyldichlorosilane and on phenylmethyldichlorosilane in presence of $FeCl_3$, $SbCl_3$ or $SbCl_5$ as catalyst at 70-120° gave chlorinated aromatic silanes containing chlorine atoms in the benzene rings [4]. These data are all that have been reported about the action of halogens on aromatic organosilicon compounds and about the products of such reactions. More detailed information, both about properties and preparative methods, is available for such compounds as p-chloro- and p-bromophenyltrichlorosilanes, di-(p-bromophenyl)-dichlorosilane, which have been synthesized with the help of appropriate organomagnesium compounds [2,5]. But the latter route cannot lead to aromatic silanes containing one or more halogen atoms in the nucleus.

We have undertaken an investigation of the halogenation of some aromatic silanes and of the properties of the resultant halo derivatives because the above survey shows the extent to which this field of chemistry has been neglected. In this paper we describe the results of syntheses of bromo derivatives of phenyltrichlorosilane. Bromination of phenyltrichlorosilane was performed in presence of the usual catalysts employed in halogenation of aromatic compounds (metallic iron, $SbCl_3$). It was established that the action of bromine on phenyltrichlorosilane in presence of metallic iron is accompanied bya vigorous exothermic reaction. At 45-50° the bromination proceeds fairly intensively and the bromine is completely taken up by the reaction mixture. Using a phenyltrichlorosilane/bromine ratio (molar) of 1:0.76, the main reaction product is monobromophenyltrichlorosilane, which is obtained in a yield of 90% of the theoretical, calculated on the reacted phenyltrichlorosilane:

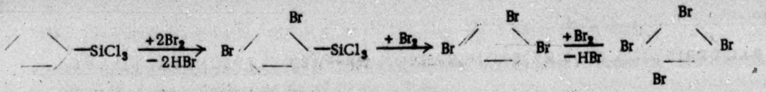
$$C_6H_5SiCl_3 + Br_2 \longrightarrow C_6H_4BrSiCl_3 + HBr.$$

Continuance of bromination at the same temperature (molar ratio of reactants 1:1.82) leads to formation of dibromophenyltrichlorosilane in a yield of about 70% of the theoretical (with an over-all yield of about 80% based on the bromophenyltrichlorosilanes). A distinguishing feature of the latter reaction is that substitution is accompanied by a secondary reaction involving cleavage of products at the Si—C bond. The cleavage products are, on the one hand, a silicon-containing compound (apparently $SiCl_3Br$) and, on the other hand, a brominated benzene (p-dibromobenzene, isolated pure). Consequently the bromination of phenyltrichlorosilane at this stage proceeds according to the scheme:

$$C_6H_4BrSiCl_3 + Br_2 \begin{array}{l} \nearrow C_6H_3Br_2SiCl_3 + HBr \text{ (main reaction)} \\ \searrow SiCl_3Br + p\text{-}C_6H_4Br_2 \text{ (side reaction)} \end{array}$$

Due to the occurrence of the side reaction (destructive bromination) the yield of dibromophenyltrichlorosilane is reduced.

Destructive bromination proved to be the sole reaction taking place in attempts to prepare tribromophenyltrichlorosilane. In this case the bromination proceeds at a considerably lower speed than in the preparation of the mono- and dibromo- derivatives, and necessitates prolonged action of excess of bromine on phenyltrichlorosilane at 80-90°. Thus, with a ratio of reactants of 1:3.25 the principal reaction product is 1,2,4,5-tetrabromobenzene, side by side with dibromophenyltrichlorosilane which is obtained in a yield of 24.6% of the theoretical. No trace of tribromophenyltrichlorosilane could be found among the reaction products. Formation of 1,2,4,5-tetrabromobenzene may be represented by the following scheme:



This scheme could be confirmed to some extent by experiments on the bromination of 2,4-dibromophenyltrichlorosilane. Thus, on conducting the bromination of 2,4-dibromophenyltrichlorosilane (molar ratio of $C_6H_3Br_2SiCl_3/Br_2$ approx. 1:2) in presence of metallic iron at 90-95°, only a small amount of 2,4-dibromo-derivative is recovered unchanged; in this case the main reaction product is 1,2,4,5-tetrabromobenzene, formed in good yield.

The complete absence from the reaction products of tribromophenyltrichlorosilane as well as of 1,2,4,6-tetrabromobenzene permits the assumption that the Si—C bond is cleaved in dibromophenyltrichlorosilane under the action of bromine and that tribromophenyltrichlorosilane is apparently not formed, even as an intermediate product. Attempts to obtain tribromophenyltrichlorosilane by bromination of 2,4-dibromophenyltrichlorosilane in milder conditions (in carbon tetrachloride solution at 75-77°) did not attain their objective (substantially the whole of the dibromophenyltrichlorosilane was recovered unchanged). A positive result did not follow the bromination of the dibromo-derivative in presence of 2% antimony trichloride as catalyst even at 180-200°.

Consequently, the course of the bromination of phenyltrichlorosilane in presence of catalysts depends on the nature of the catalyst, on the thermal conditions of the reaction and on the ratio of reactants. It should be noted that in the absence of catalysts the bromination of phenyltrichlorosilane does not take place even at 170-180° (in a sealed tube).

The structure of the synthesized bromo derivatives of phenyltrichlorosilane was confirmed with the help of cleavage reactions in presence of aluminum chloride and bromine water. The first of these reactions was previously reported by various authors [6] for unsubstituted aromatic silanes such as tetraphenylsilane, triethylphenylsilane and diphenyldichlorosilane. But the cleavage of the Si—C bond with the help of bromine water has only been described in the case of quaternary aromatic nitro-substituted organosilicon compounds [7]. In their application to bromosubstituted phenylchlorosilanes, these reactionsare here studied for the first time. In these cases the reaction proceeds in such a manner that the products of the cleavage reactions are bromo derivatives of benzene, e.g.:

$$C_6H_3Br_2SiCl_3 + AlCl_3 \xrightarrow{(5H_2O)} C_6H_4Br_2 + SiO_2 + 6HCl + Al(OH)_3$$

$$C_6H_3Br_2SiCl_3 + Br_2 + 2H_2O \longrightarrow C_6H_3Br_3 + SiO_2 + 3HCl + HBr,$$

and it is possible to evaluate their structure both in respect to the relative positions of the bromine atoms in the aromatic ring of bromophenyltrichlorosilane and in respect to the orienting effect of the silicyl chloride group. It was thus established that although the $SiCl_3$ group must, by its nature, be a meta-orienting substituent, the bromination of phenyltrichlorosilane in presence of iron leads to formation exclusively of the para-derivative. Formation of a para- and not a meta-derivative is confirmed beyond doubt by the fact that the product of cleavage of monobromophenyltrichlorosilane with bromine water (heating at 150-160° in a sealed tube) is p-dibromobenzene (yield 83% of the theoretical); further confirmation is supplied by the identity between the bromination product and the p-bromophenyltrichlorosilane prepared from p-bromophenyl magnesium bromide and silicon tetrachloride:

$$p\text{-}BrC_6H_4MgBr + SiCl_4 \longrightarrow p\text{-}BrC_6H_4SiCl_3 + MgBrCl.$$

These results clearly demonstrated an anomalous course of reactions involving substitution of hydrogen atoms by bromine atoms in the phenyltrichlorosilane ring under the action of elementary bromine in presence of a catalyst. Investigation of the structure of dibromophenyltrichlorosilane fully confirmed this fact: when the latter was cleaved with bromine water (heating at 180-190° in a sealed tube) the reaction product was 1,2,4-tribromobenzene (60% yield); cleavage of dibromophenyltrichlorosilane with aluminum chloride (using a 1:1 molar ratio of components) led to formation of m-dibromobenzene in 55% yield. These data indicate that the dibromo-derivative of phenyltrichlorosilane prepared by bromination of the latter in presence of a catalyst is 2,4-dibromophenyltrichlorosilane. Here again, therefore, we observe an anomalous orientation of the bromine atoms entering the nucleus of phenyltrichlorosilane.

EXPERIMENTAL

I. Preparation of p-bromophenyltrichlorosilane. The reaction vessel was a four-necked round-bottomed flask fitted with a mechanical stirrer, a dropping funnel, a thermometer and a reflux condenser connected to a series of absorption bottles intended for trapping the hydrogen bromide. Into this vessel was introduced 100.0 g (0.472 mole) phenyltrichlorosilane and 0.5 g powdered metallic iron (0.5% of the weight of the phenyltrichlorosilane). Addition was made to this mixture, with stirring, over a period of 1½-2 hours, of 58.0 g (0.362 mole) dry bromine (dropwise from the dropping funnel); this was 76.7% of the amount of bromine theoretically required for bromination to the monobromo-derivative. After 1-2 minutes the temperature of the reaction mass began to rise and reached 50°. Intensive bromination took place at 45-50°, and substantially the whole of the bromine entered into reaction. When all had been added, the reaction mass was heated for one hour on a water bath at 90-95° for completion of the reaction, after which a stream of dry air was passed through for removal of the residue of hydrogen bromide and unreacted bromine. The weight increase after the air-blowing was 26.1 g (against 28.6 g theoretically demanded for bromination to the monobromo-derivative in the conditions of this experiment). The amount of hydrogen bromide evolved as a result of bromination was 27.7 g.

Vacuum-distillation of the bromination product gave: 1) b.p. 68-90° (6 mm) – 26.3 g; 2) b.p. 90-115° (6 mm) – 97.2 g; flask residue about 2.0 g of dark resin.

The first fraction was mainly unchanged phenyltrichlorosilane. Redistillation of the second fraction gave 94.8 g colorless liquid with b.p. 105-109° (6 mm) which consisted of monobromophenyltrichlorosilane. Yield 69% of the theoretical, calculated on the reacted phenyltrichlorosilane.

Monobromophenyltrichlorosilane is a colorless, mobile, oily, liquid fuming in the air: b.p. 106-108° (6 mm), d^{20} 1.6771. For the purpose of determination of the bromine content, a small amount of the obtained monobromophenyltrichlorosilane was resinified by treatment with water and subjected to analysis.

Found %: Br 38.0, 38.5; Cl (hydrolysis) 36.3, 36.1. $C_6H_4BrSiO_{1.5}$. Calculated %: Br 38.4. $C_6H_4BrSiCl_3$. Calculated %: Cl (hydrolysis) 36.6.

The properties of the obtained monobromophenyltrichlorosilane were identical with those of synthetic p-bromophenyltrichlorosilane prepared from p-bromophenyl magnesium bromide and silicon tetrachloride. In addition, evidence of the structure was obtained by cleavage with bromine water in a sealed tube. Into a glass tube were introduced 2.0 g monobromophenyltrichlorosilane, 0.9 ml bromine and 1.9 ml water. The tube was heated in a tube furnace for 6 hours at 150-160°. The contents of the tube were then extracted with ether and the ether extract was washed with 10% sodium carbonate solution; the solution was then washed with water and dried over calcium chloride. From the ether extract was isolated a crystalline, white substance which was recrystallized twice from alcohol to form lustrous, white platelets with m.p. 86.2°, consisting of p-dibromobenzene (about 1.3 g). It did not depress the m.p. of p-dibromobenzene. Yield of p-dibromobenzene about 83% of the theoretical.

II. Preparation of 2,4-dibromophenyltrichlorosilane. Bromination of phenyltrichlorosilane to the dibromo derivative was performed in the same conditions as above except that the amount of bromine brought into reaction was correspondingly increased. Into a mixture of 100.0 g (0.472 mole) phenyltrichlorosilane and 0.5 g metallic, powdered iron (0.5% of the weight of the phenyltrichlorosilane) was introduced dropwise, with stirring over a period of 2½-3 hours, 138.0 g (0.862 mole) dry bromine, equivalent to 91.2% of the theoretical amount for bromination to the dibromo derivative. During the period of introduction the temperature of the reaction mass was held at 45-50°, following which the reaction was completed by heating for one hour on a water bath at 90-95°. The amount of hydrogen bromide evolved during the reaction was 57.4 g.

Vacuum-distillation of the bromination product gave: 1) b.p. 85-125° (6 mm) – 22.0 g; 2) b.p. 125-150° (6 mm) – 130.0 g; residue in flask about 2.0 g of dark resin.

On distillation of the first fraction, crystallization in the condenser occurred at the very start (needles). This fraction was treated with water and subjected to steam distillation. From the distillate was isolated a white, crystalline substance (4.0 g) which after two recrystallizations from alcohol formed white leaflets with m.p. 86.2°. This substance did not depress the m.p. of p-dibromobenzene.

Found %: Br 67.2, 67.4 (Carius method) $C_6H_4Br_2$. Calculated %: Br 67.8.

The residue in the flask (10.5 g) after the steam distillation was a light-yellow, transparent resin whose bromine and silicon contents were consistent with the formula $(C_6H_4BrSiO_{1.5})_n$. Formation of this resin would be due to saponification of the monobromophenyltrichlorosilane present in the first fraction.

Found %: Br 37.6, 37.5; Si 13.0, 12.6. $(C_6H_4BrSiO_{1.5})_n$. Calculated %: Br 38.4; Si 13.46.

Consequently the first fraction contained p-dibromobenzene in addition to monobromophenyltrichlorosilane.

Redistillation of the second fraction gave 122.0 g liquid with b.p. 143-147° (6 mm), consisting of dibromophenyltrichlorosilane. Yield 70% of the theoretical, calculated on the phenyltrichlorosilane taken in the reaction.

Dibromophenlyltrichlorosilane is a colorless, mobile, oily liquid, which fumes in the air; b.p. 144-146° (6 mm), d^{20} 1.9502. A portion of the prepared substance was analyzed for bromine by treating with water and estimating the bromine content of the resultant resin.

Found %: Br 55.4, 55.8 (Carius); Cl (hydrolysis) 28.4, 28.6. $C_6H_3Br_2SiO_{1.5}$. Calculated %: Br 55.7. $C_6H_3Br_2SiCl_3$. Calculated %: Cl (hydrolysis) 28.8.

The total yield of bromophenyltrichlorosilanes (mono- and dibromo- derivatives) was about 80% of the theoretical.

The structure of the prepared dibromophenyltrichlorosilane was confirmed by cleavage with bromine water. A sealed glass tube containing 2.0 g dibromophenyltrichlorosilane, 0.5 ml bromine and 1.2 ml water was heated for 6 hours at 180-190°. The contents of the tube were then worked up as described above. From the ether extract was isolated a crystalline compound which after two recrystallizations from alcohol-ether mixture gave white needles with m.p. 44°, consisting of 1,2,4-tribromobenzene (1.0 g) in a yield of 60% of the theoretical).

For further confirmation, the dibromophenyltrichlorosilane was cleaved with $AlCl_3$ (1:1 ratio of reactants). The reaction product (after decomposition of the reaction mass with water) was m-dibromobenzene — a liquid with b.p. 220°, solidification point 7°, and d^{20} 1.9594 (yield 55% of the theoretical).

III. Attempts to prepare tribromophenyltrichlorosilane. 1. Bromination of phenyltrichlorosilane. To a mixture of 35.0 g (0.165 mole) phenyltrichlorosilane and 0.17 g powdered metallic iron (0.5% of the weight of the phenyltrichlorosilane) was added dropwise, with stirring, 85.8 g (0.536 mole) dry bromine (silane/bromine ratio - 1:3.25). The first two-thirds of the bromine was added in the course of 1½ hours at 45-50° and substantially the whole of it entered into reaction. Since the further progress of the reaction was appreciably slowed down, the last third of the bromine was added over a period of 1½ hours at 75-80°. After the whole of the bromine had been added, the reaction was completed by heating for one hour on the water bath at 90-95°. With progressive cooling the bromination product partially crystallized. The weight increase of the reaction mass after air-blowing was 38.0 g. The amount of hydrogen bromide evolved as a result of bromination was 38.1 g (a precipitate of SiO_2 was observed in the bottle in which the hydrogen bromide was absorbed).

Vacuum-distillation of the bromination product gave: 1) b.p. 135-155° (6 mm) —20.0 g; 2) b.p. 155-165° (6 mm) —45.0 g; residue in flask about 5.0 g of dark resin.

The first fraction is an oily liquid containing a small amount of crystals (about 3 g) of tetrabromobenzene. Examination of this fraction showed it to consist mainly of dibromophenyltrichlorosilane (about 15.0 g).

The second fraction crystallized almost completely at the ordinary temperature but the crystals were permeated by an oily liquid. Two recrystallizations from dry dichloroethane (or petroleum ether) gave white needles (about 38.0 g) with m.p. 175° and the specific odor of polyhalobenzenes. Analysis revealed the absence from it of silicon and hydrolyzable chlorine, while the bromine content (Carius) corresponded to that of tetrabromobenzene.

Found %: Br 80.7, 81.0. $C_6H_2Br_4$. Calculated %: Br 81.2.

The m.p. of 175° agreed with that of 1,2,4,5-tetrabromobenzene.

2. Bromination of 2,4-dibromophenyltrichlorosilane. a) To a mixture of 20.0 g (0.054 mole) 2,4-dibromophenyltrichlorosilane (prepared as described above) and 0.1 g powdered metallic iron was added dropwise, over a period of 0.5 hours, 17.2 g (0.107 mole) dry bromine (silane/bromine ratio = approx. 1:2.0). The reaction only took place with evolution of hydrogen bromide when the mass was heated to 90-95°. Heating was therefore performed on the boiling water bath for one hour. On cooling, the bromination product crystallized.

Vacuum-distillation gave: 1) b.p. 140-160° (7 mm) —4.0 g; 2) b.p. 160-170° (7 mm) —16.0 g; residue in flask about 2 g dark resin.

The first fraction, an oily liquid partly crystallizing on cooling, was found to consist mainly of unchanged dibromophenyltrichlorosilane with an admixture of bromo-derivatives of benzene.

Redistillation of the second fraction yielded about 14.5 g colorless, transparent liquid with b.p. 163-165° (7 mm) which rapidly crystallized. Two recrystallizations from petroleum ether gave white needles melting at 175-176° (about 9.0 g). The analysis was consistent with the compound being a tetrabromobenzene. It did not depress the melting point of 1,2,4,5-tetrabromobenzene.

b) Bromination of dibromophenyltrichlorosilane did not take place on heating a mixture of 15.0 g (0.04 mole) 2,4-dibromophenyltrichlorosilane, 45.0 g carbon tetrachloride, 0.08 g iron powder and 7.7 g (0.048 mole) bromine at 75-77°. When the mixture was fractionated the dibromo compound was recovered unchanged (14.0 g).

c) Heating for two hours of a mixture of 15.0 g (0.04 mole) 2,4-dibromophenyltrichlorosilane, 0.03 g $SbCl_3$ and 9.7 g (0.06 mole) bromine at 180-200° did not result in bromination of the silane. Fractionation of the reaction mixture gave 14.5 g of the original dibromophenyltrichlorosilane.

SUMMARY

1. The following results were obtained in a study of the reaction of bromine with phenyltrichlorosilane: a) In the absence of catalyst no reaction occurs even at 200°; b) in the presence of the usual catalysts for halogenation of aromatic compounds, for example iron, ring-bromination takes place relatively easily up to formation of the dibromo-derivative. It was not possible to prepare a tribromo-derivative by bromination of phenyltrichlorosilane or of dibromophenyltrichlorosilane in presence of iron or antimony trichloride.

2. The reaction of formation of bromophenyltrichlorosilanes is accompanied by the side reaction of destructive bromination as represented by cleavage by bromine of the Si—C bonds of organosilicon compounds. It was noted that the course of this side reaction depends on the nature of the catalyst.

3. Of the products of bromination of phenyltrichlorosilane, the mono- and dibromo-derivatives were isolated in good yields and characterized in the pure form. Their structures correspond respectively to 1,4- and 1,2,4-isomers.

4. Bromination of phenyltrichlorosilane in presence of catalysts is found to proceed anomalously in respect to the orienting effect of the $SiCl_3$ group. In place of the anticipated meta-orientation there was observed the unusual ortho-para-orientation of the bromine atoms entering the nucleus.

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CARBOXYLIC ANHYDRIDES OF AMINO ACIDS AS A STRUCTURAL FRAGMENT IN THE PROTEIN MOLECULE

(Commemoration of the 60th anniversary of A. Ya. Danilevsky's theory of elementary series)

L. N. Akimova and N. I. Gavrilov

After demonstrating in a series of papers that the polypeptide theory is no longer consistent with the experimental facts [1] accumulated by numerous workers over the past 20 years, we shall now attempt on the basis of model syntheses to identify the possible fragments of the protein structure corresponding to natural proteins in properties and capable of facilitating the clarification of protein structure. These fragments include the bond reported in 1891 by the founder of Russian biochemistry, A. Ya. Danilevsky [2]. The reality of the carboanhydride bond discovered by him was experimentally established in 1924 by Fränkel [3].

By the eighties of last century a hundred years had already passed since the establishment of the elementary composition of proteins and since the significance of the amino acids for their structure had been demonstrated. At that time potein was characterized as a complex mixed anhydride of a relatively small number of amino acids (not more than twenty — Schall, Grimaux, Schützenberger). This period also marked the start of attempts to synthesize protein from amino acids. It was perfectly natural that in the attempts to gain insight into the structure of the protein molecule, investigators should work along the lines of combining amino acids among themselves in such a manner that compounds possessing all the properties of the natural products would be formed. And since a number of workers tended to characterize protein as amino acid anhydrides, it is fully understandable why the first syntheses were directed to the preparation of such anhydrides. In view of the fact that most anhydrides are prepared by removal of water, use was made of the usual methods of dehydration, consisting in the heating of the amino acid or mixtures of amino acids in glycerol or with P_2O_5, or in treatment with thionyl chloride. The first to synthesize these anhydrides was the German chemist Curtius [4]. He prepared the first anhydride $C_6H_5CONHCH_2CONHCH_2COOH$ (hippurylglycine). This synthesis was especially interesting in that hippuric acid was a member of the group of natural compounds since it is found in horses' urine. This synthesis initiated a whole series of investigations with a view to synthesis of protein. It was thus shown for the first time that amino acids can combine with one another at the substituted amino bond, subsequently named the peptide bond by Fischer.

In 1883 Curtius drew attention to the fact that the ethyl ester of glycine undergoes spontaneous transformation into glycine anhydride (diketopiperazine) and a substance giving a positive biuret reaction. For this reason the latter substance was called "biuret base". Later work by Curtius showed that if moisture was removed from the reaction mixture, the anhydride formation was inhibited and "biuret base" was the main reaction product. But Curtius' erroneous theory about the occurrence of the biuret reaction of proteins did not permit him to put forward a theory of the structure of synthetic "biuret base". And it was only after a further 21 years that this substance was conclusively identified as a pentapeptide ether.

All the above attempts at a protein synthesis were not linked by common concepts of the structure of protein. The diversity of amino acids in protein and the high molecular weight very seriously complicated the problem of elucidating the structures of proteins and have so far prevented a systematic synthesis of these compounds. Evidence of this is provided by the fact that nobody has yet (with the exception of Rinch and Talmud) presented a general theory of protein structure, discussions ranging only round protein fragments and the indeterminate protein structures proposed by Astbury and Pauling.

Credit for the first attempt to establish the structure of a concrete fragment of the molecular structure belongs to A. Ya. Danilevsky. He was the first to approach the problem of protein structure as an organic chemist. In attempting to establish the fundamental structural units of proteins, Danilevsky concentrated on the fact that in the decomposition of proteins in the living organism the end product of metabolism is urea; moreover, the products of digestion of proteins with gastric juice — peptone — give a pink color on addition of $CuSO_4$ and NaOH. The same color is given with these reagents by the compound formed by melting of urea (biuret). This justified Danilevsky in proposing that the molecular grouping of biuret in the form of molecules or of —NHCONHCONH—

residues is a precursor in the structure of protein. Danilovsky writes as follows: "...in the protein molecule the 'carboazoto' group is not actually the biuret residue, but it is a complex of atoms of carbon and nitrogen which have the same intramolecular behavior as in biuret. I therefore suggest that the biuret group of the protein molecule has the form −NHCONHCONH−".

It should be noted that at that time the biuret reaction of organic compounds, which had been mainly studied with diamides, was not associated with the peptide structure of the protein molecule, and therefore also in A. Ya. Danilevsky's considerations this reaction is not identified with the polypeptide structure but with the presence in protein of biuret and amides. It must be emphasized that only E. Fischer introduced the biuret reaction as a characteristic of modern ideas of protein structure involving the presence of polypeptides. While suggesting the presence in protein of individual molecules (or, more correctly, residues) of biuret, Danilevsky sought confirmation of this suggestion by attempting to obtain biuret by hydrolyzing protein. All his efforts, however, were in vain, and his tentative suggestion was verified only after ureide acids − citrullin, etc. − had been found among the breakdown products of protein.

In what way did A. Ya. Danilevsky sense the relation between the biuret-containing groups and the main structural units of protein, i.e. amino acids ? To what extent did his proposed structural micro-fragments correspond to our concepts of protein structure ? A great deal has changed since that time. The polypeptide theory of Hofmeister and Fischer was developed and discarded, the diketopiperazine theory of Zelinsky and Sadikov had a salutary influence, and the ideas expounded by A. Ya. Danilevsky were not fully confirmed. But Danilevsky's ideas about elementary series have developed into the concept of the monomer in the protein structure.

Now the biuret group was the precursor of the discovery of the ureido acids. The anhydride bonds, simple and mixed, permitted the prediction of a whole series of structures found in other investigations, and their confirmation and development (the prosthetic group, the C−O−C− anhydride bond, the CO−NH−peptide bond; utilization of the biuret reaction as a criterion of structure). But A. Ya. Danilevsky was cautious. This is what he writes about his structures: "... each elementary series constitutes a prototype of protein substance, but is still not protein substance..."

What, then does Danilevsky's elementary series consist of? In his opinion the individual biuret residues are combined with amino acids and prosthetic groups to form structural units designated by him the "elementary series of the protein molecule". The general formula of such series has the form Y−NHCONHCONH−R, where R is an amino acid residue and Y is a prosthetic group of protein and non-protein origin (carbohydrate, alkaloid, amino acid, etc.).

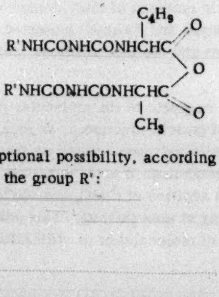
For example:

$$\underbrace{Y{-}NHCONHCONH}_{\text{biuret group}}{-}\underbrace{CH_2{-}COOH}_{\text{glycolic group}}$$

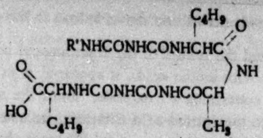
$$\underbrace{Y{-}NHCONHCONH}_{\text{biuret group}}{-}\underbrace{C_2H_4{-}COOH}_{\text{alanine group}}$$

It is interesting that in this form of the compounds the amide group of biuret is simultaneously the α-amino group of the amino acid.

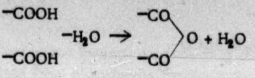
Moreover, according to Danilevsky this fragment is linked to another fragment by means of the anhydride bond and we obtain the transition to the macrostructure:



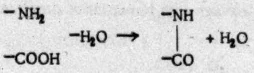
An exceptional possibility, according to Danilevsky, is the formation of an anhydride bond at an amino acid entering at the group R':



Danilevsky thus suggested the existence in the protein molecule of two types of anhydride bonds: one type — the predominating one — mainly in the form of a simple anhydride:



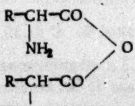
and the other possible one in the form of a mixed anhydride



This hypothesis of the occurrence of two possible types of bond in the protein molecule was supported, in Danilevsky's opinion, by the specificity of the medium necessary for the activity of ferments (acid for pepsin, and alkaline for trypsin). We may note that Danilevsky did not ascribe special significance to the mixed anhydrides, and he considered that they could be present in proteins but with a lesser degree of probability than the simple anhydrides. In this resides the fundamental distinction between Danilevsky's ideas about protein structure and the polypeptide theory which regards a bond of the mixed linear anhydride type as the principal and sole bond in proteins.

Special attention is merited by Danilevsky's concept of the anhydride bond in proteins between the microfragments which enclose the biuret group. Still another service of Danilevsky was that he was the first to approach the problem analytically and to base his hypotheses on the facts accumulated at that time, so that he was able to conclude that the protein molecule comprises microfragments which are linked to form a macromolecule. In the nineties of the last century it was clearly demonstrable that the analytical method permitted the inference that anhydrides entered into the structure of protein.

In the twenties of this century Fränkel [3] fermented protein with trypsin and isolated anhydrides of amino acids such as tyrosine, tryptophane and others, consistent with Danilevsky's ideas. When he treated protein with pancreatin he observed the formation of free tryptophane (test by reaction with bromine water). The free amino acid disappears on continuation of the treatment of protein with pancreatin or with pure preparations of trypsin. The author explains this change by the synthesizing action of the ferment; he draws attention to the following possible couplings or combinations of amino acids with one another: dipeptide — due to detachment of one molecule of H_2O; anhydride (a), also formed with loss of one molecule of H_2O; and cyclic anhydride, formed with separation of 2 molecules of H_2O. Analysis of the isolated Fränkel compounds showed that they contained two free amino groups (van Slyke determination) and that carboxyl groups were absent (Sörenson's formol titration). All this is evidence for an anhydride structure of the type of a. Fränkel's isolation of the anhydrides of tryptophane and tyrosine from proteins marked the discovery of a new function of trypsin (up to then trypsin had only been known to cleave peptide bonds), involving the anhydridization of amino acids of identical structures. Formation of mixed anhydrides was not observed during the process. Fränkel's detection of amino acid anhydrides in proteins and the elucidation of their structure by analysis permitted the prediction of the natural existence of this type of bond.

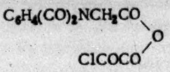


(a)

In recent years investigations have been made, in particular, of a whole series of reactions leading to the synthesis of a carboanhydride bond of a mixed type [5]. These reactions were mainly performed with N-substituted amino acids (carbobenzoxy, phthaloyl-) which were converted into mixed anhydrides under the action of ethyl chloroformate in presence of a tertiary amine in dioxane or chloroform. The resultant mixed anhydrides were not isolated but immediately entered into reaction with the amino acid to form compounds with a peptide bond. This method provided a new route to the synthesis of peptides.

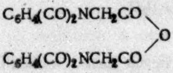
It is interesting to note that if Danilevsky had realized his structure experimentally, he would indisputably have been the founder of the theory of the peptide structure of protein. For the action of simple anhydrides, similar to those indicated by Danilevsky, on amino acids leads (as will be shown below) to the synthesis of peptides.

In our preceding studies [6] we demonstrated the reality of the N-aminoacyl bond. In the further development of this type of compound of diketopiperazine with amino acids, it appeared to us of great interest to effect a direct synthesis of N-aminoacyldiketopiperazines containing a tripeptide. Since the action of phosphorus pentachloride on N-substituted tripeptides does not lead to the desired acid chlorides, we attempted to prepare the latter with the help of other chlorinating media. As will be shown below, we used thionyl chloride and oxalyl chloride. After unsuccessful attempts to synthesize the acid chlorides of di- and tripeptides with the help of thionyl chloride, we proceeded to investigate the chlorination reaction with oxalyl chloride. In place, however, of the anticipated acid chlorides either we obtained mixed anhydrides:



$$\begin{matrix} C_6H_4(CO)_2NCH_2CO\diagdown & \\ & O \\ ClCOCO\diagup & \end{matrix}$$

or else reactions with oxalyl chloride led to water cleavage with formation of simple anhydrides:



$$\begin{matrix} C_6H_4(CO)_2NCH_2CO\diagdown & \\ & O \\ C_6H_4(CO)_2NCH_2CO\diagup & \end{matrix}$$

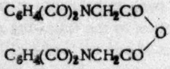
Since these simple anhydrides (judging by the studies of Danilevsky and Fränkel) can play a large part in the structure of protein, we began a study of the conditions of their formation and an investigation of their properties.

EXPERIMENTAL

I. Preparation of Simple Amino Acid Anhydrides from Mixed Anhydrides.

1. Chlorination of phthaloyl-glycine with oxalyl chloride in benzene. To 2 g phthaloyl-glycine in a Gavrilov tube was added 2.5 g oxalyl chloride (2 moles) and 15 ml dry benzene. Heating was carried out for 48 hours, during which period no visible changes were observed. At the end of the reaction, the precipitate was filtered and washed with benzene. After recrystallization from nitrobenzene the substance melted at 215°. The Beilstein test was negative. Yield 1.8 g (99%). The substance was assumed to be phthaloyl-glycine anhydride. We tested this assumption by carrying out the acylation of diketopiperzine.

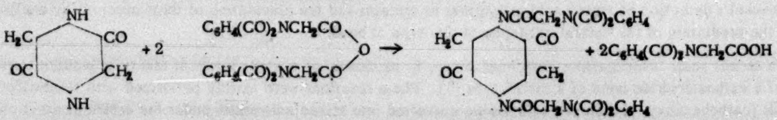
Suggested formula – Phthaloyl-glycine anhydride



$$\begin{matrix} C_6H_4(CO)_2NCH_2CO\diagdown & \\ & O \\ C_6H_4(CO)_2NCH_2CO\diagup & \end{matrix}$$

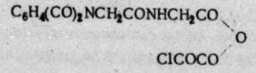
Found %: C 61.30, 61.49; H 3.36, 3.55; N 6.95, 7.14. $C_{20}H_{12}O_7N_2$. Calculated %: C 61.22; H 3.06; N 7.14.

1.1 g diketopiperazine, finely pulverized, was mixed with 3.9 g (2 moles) of the prepared phthaloyl-glycine anhydride and 15 ml nitrobenzene, and the mixture was heated on a glycerol bath at 140°. All had dissolved after 45 minutes. A precipitate came down on cooling; its properties (m.p. 385° and a positive result in the tripeptide biuret reaction after standing with caustic alkali) indicated its identity with the previously prepared N,N'-phthaloylglycyldiketopiperzaine [6]. Phthaloyl-glycine was isolated from the filtrate.



2. Chlorination of phthaloyl-glycylglycine with oxalyl chloride in benzene. 1.3 g phthaloyl-glycylglycine and 1.3 g oxalyl chloride were placed in a Gavrilov tube and 25 ml dry benzene was added. The reaction mixture was heated for 6 hours over a burner and left overnight. The precipitate was filtered and washed with benzene. The product contained halogen. It was purified by treatment with acetone, during which process a very small proportion dissolved. The insoluble residue was transferred to a flask with a reflux condenser and heated in xylene until dissolved.

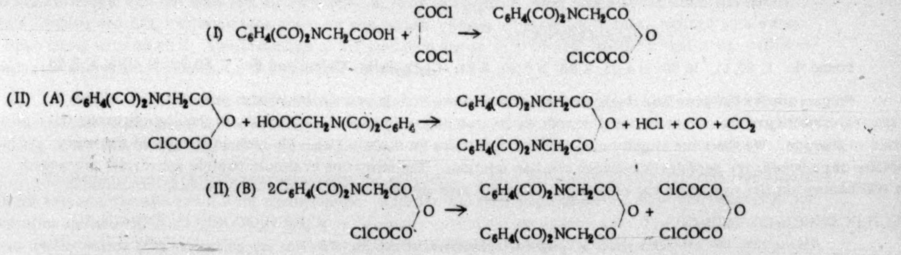
additions of xylene being made from time to time. The hot xylene solution was filtered from the insoluble residue. When the xylene solution was cooled it deposited uniform microscopic needles. The substance was insoluble in hot water, alcohol and ether, soluble in acetone; it was recrystallized from nitrobenzene and xylene; m.p. 220° with decomposition. The same substance came down from the acetone filtrate. On the basis of analysis this compound was assigned the structure of the mixed anhydride:



$$\begin{array}{l} C_6H_4(CO)_2NCH_2CONHCH_2CO \\ \qquad\qquad\qquad\qquad\qquad\quad \rangle O \\ \qquad\qquad\qquad\quad ClCOCO \end{array}$$

Found %: C 47.53, 47.47; H 2.41, 2.47; N 7.79; Cl 10.10. $C_{14}H_9O_7N_2Cl$. Calculated %: C 47.65; H 2.55; N 7.94, Cl 10.07.

This experiment enabled us to put forward the following mechanism of formation of the previously prepared phthaloyl-glycine anhydride, isolated from experiment 1 through the stage of formation of the mixed phthaloyl-glycine-oxalyl anhydride:



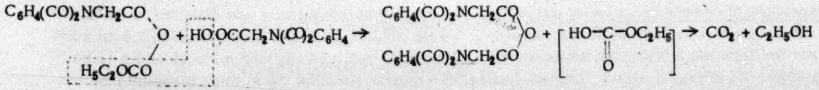
$$\text{(I)}\quad C_6H_4(CO)_2NCH_2COOH + \begin{array}{c} COCl \\ | \\ COCl \end{array} \rightarrow \begin{array}{l} C_6H_4(CO)_2NCH_2CO \\ ClCOCO \end{array}\rangle O$$

$$\text{(II) (A)}\quad \begin{array}{l} C_6H_4(CO)_2NCH_2CO \\ ClCOCO \end{array}\rangle O + HOOCCH_2N(CO)_2C_6H_4 \rightarrow \begin{array}{l} C_6H_4(CO)_2NCH_2CO \\ C_6H_4(CO)_2NCH_2CO \end{array}\rangle O + HCl + CO + CO_2$$

$$\text{(II) (B)}\quad 2\begin{array}{l} C_6H_4(CO)_2NCH_2CO \\ ClCOCO \end{array}\rangle O \rightarrow \begin{array}{l} C_6H_4(CO)_2NCH_2CO \\ C_6H_4(CO)_2NCH_2CO \end{array}\rangle O + \begin{array}{l} ClCOCO \\ ClCOCO \end{array}\rangle O$$

The experiments lead to the conclusion that the synthesis of simple amino acid anhydrides proceeds through the stage of the mixed anhydrides. This enabled us to make use of the recently prepared mixed amino acid anhydrides for the synthesis of simple amino acid anhydrides.

3. Preparation of phthaloyl-glycine anhydride. 0.84 g phthaloyl-glycine was dissolved in 10 ml absolute dioxane and 0.4 ml triethylamine was added. After cooling with water to 10°, addition was made of 0.4 ml ethyl chloroformate. After 10 minutes addition was made to the solution of 0.84 g phthaloyl-glycine in 10 ml absolute dioxane. Evolution of CO_2 took place. After an hour the precipitate was filtered off, washed three times with alcohol and then with ether. By its properties and m.p. (215°) the precipitate was identified as phthaloyl-glycine anhydride. It did not depress the melting point of a specimen of the above-described phthaloylglycine anhydride. Yield 1.5 g (93% of the theoretical). Formation of phthaloylglycine anhydride proceeds according to the following scheme:

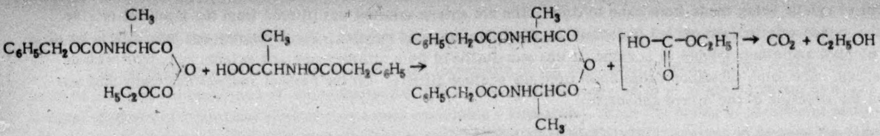


$$\begin{array}{l} C_6H_4(CO)_2NCH_2CO \\ H_5C_2OCO \end{array}\rangle O + HOOCCH_2N(CO)_2C_6H_4 \rightarrow \begin{array}{l} C_6H_4(CO)_2NCH_2CO \\ C_6H_4(CO)_2NCH_2CO \end{array}\rangle O + \left[\begin{array}{c} HO-\underset{\underset{O}{\|}}{C}-OC_2H_5 \end{array}\right] \rightarrow CO_2 + C_2H_5OH$$

4. Preparation of carbobenzoxyalanine anhydride. 0.94 g carbobenzoxyalanine was dissolved in 5 ml absolute dioxane and 0.45 g triethylamine was added. While cooling with water, addition was made to the solution of 0.4 ml ethyl chloroformate and the mass was stood at room temperature for 10 minutes. Addition was then made of 0.94 g carbobenzoxyalanine dissolved in 5 ml absolute dioxane. The mixture was left for an hour. No visible changes appeared in the precipitate and CO_2 was evolved. After an hour the precipitate was filtered and washed a few times with alcohol and then with ether. The product was recrystallized from nitrobenzene: m.p. 143°. The crystalline form (squares) is very characteristic.

Found %: C 61.79, 61.73; H 5.65, 5.61; N 6.50, 6.60. $C_{22}H_{24}O_7N_2$. Calculated %: C 61.69; H 5.61; N 6.54.

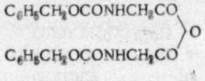
Formation of carbobenzoxyalanine anhydride may be represented by the following scheme:



$$\left.\begin{matrix}C_6H_5CH_2OCONHCH(CH_3)CO\\H_5C_2OCO\end{matrix}\right\rangle O + HOOCCH(CH_3)NHOCOCH_2C_6H_5 \rightarrow \left.\begin{matrix}C_6H_5CH_2OCONHCH(CH_3)CO\\C_6H_5CH_2OCONHCH(CH_3)CO\end{matrix}\right\rangle O + \left[HO-\overset{\displaystyle O}{\overset{\|}{C}}-OC_2H_5\right] \rightarrow CO_2 + C_2H_5OH$$

5. Preparation of carbobenzoxyglycine anhydride. 1.04 g carbobenzoxyglycine was dissolved in 5 ml absolute dioxane and 0.6 ml triethylamine was added. While cooling with water, 0.54 g ethyl chloroformate was added and the mixture left for 10 minutes at room temperature, after which 1.04 g carbobenzoxyalanine dissolved in 5 ml absolute dioxane was added. The mixture was left for an hour. Evolution of CO_2 took place. After an hour the precipitate was filtered and washed with alcohol and then with ether. The product melts at 114° after recrystallization from nitrobenzene and has the appearance of hexagonal prisms under the microscope. Yield 1.0 g or 50% of theory.

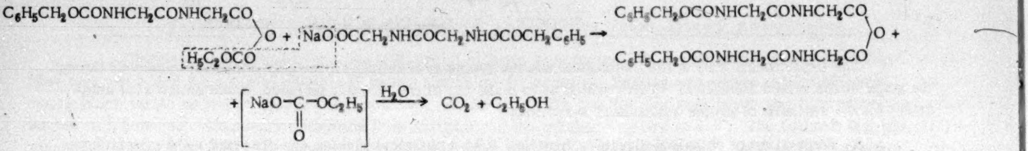
Proposed formula



$$\left.\begin{matrix}C_6H_5CH_2OCONHCH_2CO\\C_6H_5CH_2OCONHCH_2CO\end{matrix}\right\rangle O$$

Found %: C 60.11, 60.00; H 4.95, 4.86; N 6.90, 6.84. $C_{20}H_{20}O_7N_2$. Calculated %: C 59.99; H 4.99; N 7.00.

Preparation by the described method of the corresponding simple peptide-anhydrides was complicated due to the sparing solubility of the carbobenzoxy dipeptide in dioxane and the complete insolubility of the carbobenzoxy tripeptide in dioxane. We therefore slightly modified the conditions for this reaction. We took advantage of the ready solubility of carbobenzoxy peptides in aqueous alkaline solutions. The formation of simple peptide anhydrides proceeded by a mechanism similar to that for the preparation of amino acid anhydrides, i.e.:



$$\left.\begin{matrix}C_6H_5CH_2OCONHCH_2CONHCH_2CO\\H_5C_2OCO\end{matrix}\right\rangle O + NaOOCCH_2NHCOCH_2NHOCOCH_2C_6H_5 \rightarrow \left.\begin{matrix}C_6H_5CH_2OCONHCH_2CONHCH_2CO\\C_6H_5CH_2OCONHCH_2CONHCH_2CO\end{matrix}\right\rangle O + \left[NaO-\overset{\displaystyle O}{\overset{\|}{C}}-OC_2H_5\right] \xrightarrow{H_2O} CO_2 + C_2H_5OH$$

This mechanism was checked by carrying out the preparation of carbobenzoxyglycine anhydride, previously prepared by us by performing the synthesis in dioxane. And it transpired that this replacement of dioxane by aqueous alkali not only directs the reaction in the required direction but also accelerates it. This reaction proceeds instantaneously in presence of NaOH. In addition, the working-up of the reaction products is greatly simplified, and the main product (in the case of carbobenzoxyglycine anhydride) is obtained in high yield and maximum purity (carbobenzoxyglycine anhydride melts at 119° without recrystallization), whereas the m.p. after repeated recrystallization of the carbobenzoxyglycine anhydride prepared in a medium of dioxane did not exceed 114°.

6. Preparation of carbobenzoxyglycine anhydride.* 4.18 g carbobenzoxyglycine was dissolved in 20 ml absolute dioxane and 2.4 ml isobutyldimethylamine was added. To the solution (cooled to 10°) was added 1.9 ml ethyl chloroformate and the mass was left at room temperature for 10 minutes. Addition was then made of 4.18 g carbobenzoxyglycine in 20 ml 1 N caustic alkali. After an interval of 5 minutes (to allow the frothing to subside) the precipitate was filtered, washed three times with water (to dissolve the amine hydrochloride); with alcohol (to remove unreacted carbobenzoxyglycine) and with ether. After drying in a vacuum desiccator the substance melted at 119°. Yield 6.5 g or 81% of the theoretical. Concentration of the aqueous alcoholic mother liquor yielded a further 1 g of

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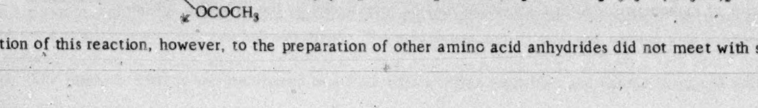
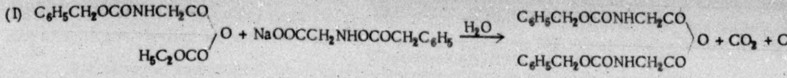
* In 1950 Wieland and co-workers obtained carbobenzoxyglycine anhydride by heating carbobenzoxyglycine acetate in benzene to 40°. This product melted at 118° after recrystallization (instead of at 119° in our reaction conditions and without recrystallization). The authors propose the following reaction mechanism:



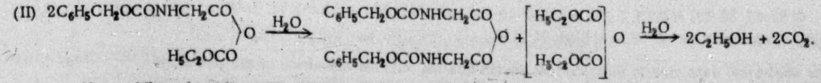
$$2C_6H_5CH_2OCO-\overset{H}{\overset{|}{N}}CH_2C\begin{matrix}\nearrow O\\ \searrow OCOCH_3\end{matrix} \rightarrow C_6H_5CH_2OCO\overset{H}{\overset{|}{N}}CH_2COOOCCH_2\overset{H}{\overset{|}{N}}OCOCH_2C_6H_5 + (CH_3CO)_2O.$$

Application of this reaction, however, to the preparation of other amino acid anhydrides did not meet with success.

substance. The reaction probably proceeds according to the following equations:



$$\text{(I)}\quad \begin{matrix}C_6H_5CH_2OCONHCH_2CO\\ H_5C_2OCO\end{matrix}\Big\rangle O + NaOOCCH_2NHOCOCH_2C_6H_5 \xrightarrow{H_2O} \begin{matrix}C_6H_5CH_2OCONHCH_2CO\\ C_6H_5CH_2OCONHCH_2CO\end{matrix}\Big\rangle O + CO_2 + C_2H_5OH$$



$$\text{(II)}\quad 2\begin{matrix}C_6H_5CH_2OCONHCH_2CO\\ H_5C_2OCO\end{matrix}\Big\rangle O \xrightarrow{H_2O} \begin{matrix}C_6H_5CH_2OCONHCH_2CO\\ C_6H_5CH_2OCONHCH_2CO\end{matrix}\Big\rangle O + \left[\begin{matrix}H_5C_2OCO\\ H_5C_2OCO\end{matrix}\right] O \xrightarrow{H_2O} 2C_2H_5OH + 2CO_2.$$

Note. When the substance with m.p. 119° was recrystallized from nitrobenzene, it had a m.p. 114°, indicating decomposition.

The following experiment showed, however, that the synthesis of carbobenzoxyglycine anhydride can take place in two stages on condition that an aqueous medium is used. 2.14 g carbobenzoxyglycine was dissolved in 10 ml absolute dioxane and 1.2 ml isobutyldimethylamine. While cooling with water, addition was made of 0.95 ml ethyl chloroformate and the mass left for 10 minutes at room temperature, after which 10 ml water was added. Violent frothing and CO_2 evolution took place for one minute. The precipitate was filtered, washed with water, and three times with alcohol. The properties of the substance and its m.p. of 119° indicated that it was carbobenzoxyglycine anhydride. Yield 0.5 g or 25% of the theoretical.

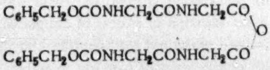
On the basis of the above facts we must regard the formation of carbobenzoxyglycine anhydride in an aqueous medium as the result of two reactions I and II (this is evidenced also by the yield of carbobenzoxyglycine anhydride which in water is 81% and in dioxane is 50%).

7. Preparation of carbobenzoxyglycylglycine anhydride. 0.66 g carbobenzoxyglycylglycine was dissolved in 10 ml absolute dioxane and 0.5 ml triethylamine. Addition was then made of 0.3 ml ethyl chloroformate, followed after an interval of 10 minutes by 0.66 g carbobenzoxyglycylglycine dissolved in 10 ml absolute dioxane and 0.5 ml triethylamine (for increasing the solubility of the carbobenzoxy dipeptide). After one hour the precipitate was filtered off and washed first with alcohol and then with ether. The substance (dried in a vacuum desiccator) melted at 146°. The substance with m.p. 146° was treated with boiling ethanol in a beaker and then filtered and washed on the filter several times with alcohol. Under the microscope the filtrate crystallizes in homogeneous needles which settle when ether is added. The alcoholic filtrate was precipitated with ether. The resultant substance was the original carbobenzoxyglycylglycine.

The precipitate which had been treated with alcohol and was insoluble in it was recrystallized from nitrobenzene. M.p. 148°.

Note. Carbobenzoxyglycylglycine is soluble in boiling dioxane, in alcohols and in hot nitrobenzene. It comes down from hot ethyl alcohol in the form of needles. The obtained substance is absolutely insoluble in alcohol. It crystallizes from nitrobenzene in characteristic semilyrate crystals.

Proposed formula:



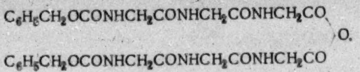
$$\begin{matrix}C_6H_5CH_2OCONHCH_2CONHCH_2CO\\ C_6H_5CH_2OCONHCH_2CONHCH_2CO\end{matrix}\Big\rangle O$$

Found %: C 56.14, 55.98; H 5.25, 5.15; N 10.85, 10.81. $C_{24}H_{26}O_9N_4$. Calculated %: C 56.03; H 5.06; N 10.89.

Determination of the acid equivalent. 0.0531 g substance: 0.05 ml 0.1 N NaOH. After standing for 24 hours the solution was acidified. Hydrolysis consumed 0.15 ml 0.1 N NaOH in the titration. Corresponding to 11.3 equivalents.

8. Preparation of the carbobenzoxy tripeptide anhydride. 0.32 g carbobenzoxy tripeptide was dissolved in 10 ml absolute dioxane and 0.2 ml triethylamine. Addition was then made of 0.11 g ethyl chloroformate. After standing for 10 minutes, addition was made to the mixture of 0.32 g carbobenzoxy tripeptide in 10 ml dioxane and 0.2 ml triethylamine. After standing for two hours, the precipitate was filtered off and washed with dioxane, alcohol (several times) and ether. The substance dried in a desiccator had m.p. 156°. In order to free the reaction product from the original carbobenzoxy tripeptide, aqueous alcohol and neutral red were added to it. It was titrated with 0.1 N NaOH and the insoluble precipitate was filtered off and washed with water and (repeatedly) with alcohol to remove the color. The insoluble precipitate was analyzed.

Proposed formula:



$$\left.\begin{array}{l}C_6H_5CH_2OCONHCH_2CONHCH_2CONHCH_2CO\\C_6H_5CH_2OCONHCH_2CONHCH_2CONHCH_2CO\end{array}\right\rangle O.$$

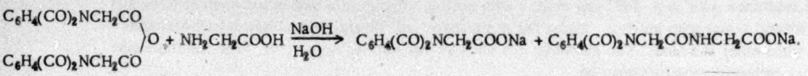
Found %: C 52.65, 52.73; H 5.19, 5.31; N 13.30, 13.35; incombustible residue 1.71, 1.68. $C_{28}H_{32}O_{11}N_6$. Calculated %: C 53.5; H 5.09; N 13.38.

Note: The analytical data clearly indicate that we are dealing with the anhydride of the phthaloyl tripeptide contaminated with Ba, since the incombustible residue amounts to 1.7% of the total weight. Barium was present in the titrated alkali solution. It is therefore necessary to take into consideration the separation of the carbobenzoxy tripeptide anhydride from the original carbobenzoxy tripeptide. We could probably achieve complete separation of the anhydride from the original peptide by titration with alkali, but only if barium was absent from the alkali.

II. Synthesis of Peptides with the Help of Simple Amino Acid Anhydrides.

1. Synthesis of phthaloylglycylglycine. 1 g phthaloylglycine anhydride was mixed with 0.27 g glycine in 15 ml water and 0.28 g NaOH (2 moles NaOH per mole of formed phthaloyl dipeptide and per mole of phthaloylglycine resulting from the reaction). The suspension was shaken on the machine for an hour; part of the precipitate failed to dissolve. An additional 0.1 g NaOH was then added and the whole dissolved on further shaking. At the end of the reaction the solution was neutralized with hydrochloric acid until the reaction was weakly acid, and evaporated to dryness in vacuum. The residue was taken up with water, filtered, and washed with water until the wash liquors gave a negative reaction for halogen. The precipitate then was washed three times with alcohol (phthaloylglycine was detected in the filtrate) and then with ether. The substance, dried in a vacuum desiccator, melts at 231° and gives a dipeptide biuret reaction. Analysis indicates that the substance is phthaloylglycylglycine [7]. Yield 0.35 g or 53% of the theoretical.

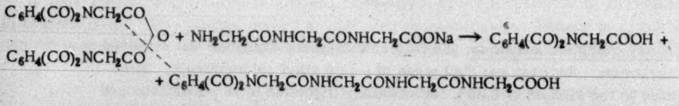
The reaction proceeds according to the scheme:



$$\left.\begin{array}{l}C_6H_4(CO)_2NCH_2CO\\C_6H_4(CO)_2NCH_2CO\end{array}\right\rangle O + NH_2CH_2COOH \xrightarrow[H_2O]{NaOH} C_6H_4(CO)_2NCH_2COONa + C_6H_4(CO)_2NCH_2CONHCH_2COONa.$$

2. Synthesis of phthaloylglycylglycylglycylglycine. 1 g of phthaloylglycine anhydride was mixed with 0.65 g glycylglycylglycine dissolved in 15 ml water with 0.28 g NaOH. The reaction mixture was agitated on the shaker for an hour; a very small amount failed to dissolve; a further 0.05 g NaOH was therefore added. Vigorous shaking resulted in a transparent solution. After neutralization, the solution was evaporated to dryness in a vacuum. The precipitate, brought on to a filter with alcohol, was insoluble in organic solvents and slightly soluble in water. After treatment with water (for removal of NaCl) the precipitate was washed with alcohol. The alcoholic filtrate proved to be entirely free from any compound.

When the biuret reaction was performed with the precipitate, a clear red color was developed in the first instant of addition of the copper solution, and only after addition of excess of copper did a violet color appear. This precipitate is inevitably a mixture of the formed phthaloyl tetrapeptide and the original tripeptide. But due to their extraordinarily similar solubility characteristics (soluble in water, insoluble in organic solvents), this mixture could not be separated into its components. However, the separation from the alcoholic filtrate (when working up the main precipitate) of phthaloylglycine clearly points to the following course of the reaction:



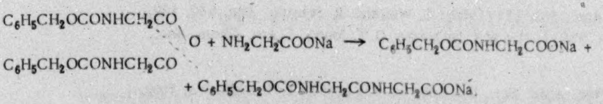
$$\left.\begin{array}{l}C_6H_4(CO)_2NCH_2CO\\C_6H_4(CO)_2NCH_2CO\end{array}\right\rangle O + NH_2CH_2CONHCH_2CONHCH_2COONa \longrightarrow C_6H_4(CO)_2NCH_2COOH + \\ + C_6H_4(CO)_2NCH_2CONHCH_2CONHCH_2CONHCH_2COOH$$

It was consequently impossible to isolate the phthaloyl tetrapeptide from this reaction. We only established its undoubted formation from the evidence of the red biuret reaction.

3. Synthesis of carbobenzoxyglycylglycine. 0.37 g glycine was dissolved in 10 ml (2 moles) 1 N NaOH and 2 g carbobenzoxyglycine anhydride was added. After 15 minutes' standing the perfectly transparent solution

was acidified with hydrochloric acid. The resultant precipitate was filtered off and washed first with water and then with alcohol (3 times)(for separation from carbobenzoxyglycine) and ether. After drying in a vacuum desiccator, the substance melted at 178°; its other properties (positive biuret reaction of the dipeptide type, insolubility in water and poor solubility in alcohol) identified it with carbobenzoxyglycylglycine [8]. Yield 1.0 g or 75% of the theoretical.

Formation of carbobenzoxyglycylglycine proceeds according to the following scheme:



$$\begin{matrix} C_6H_5CH_2OCONHCH_2CO \\ C_6H_5CH_2OCONHCH_2CO \end{matrix}\Big\rangle O + NH_2CH_2COONa \rightarrow C_6H_5CH_2OCONHCH_2COONa + C_6H_5CH_2OCONHCH_2CONHCH_2COONa.$$

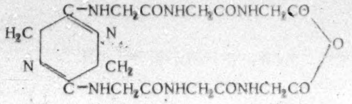
4. Synthesis of carbobenzoxyglycylglycylglycine. To 4 g carbobenzoxyglycine anhydride was added 1.32 g glycylglycine dissolved in 10 ml 1 N NaOH (2 moles). After complete solution, acidification was effected with hydrochloric acid until weakly acidic. The resultant precipitate was filtered off and washed with water until the residue reacted negatively to the ninhydrin test; the residue was then treated on the filter with alcohol (carbobenzoxyglycine was separated from the filtrate). After drying in a vacuum desiccator the substance melted at 196°. Its properties (complete insolubility in alcohol, biuret reaction of the tripeptide type) identified it with carbobenzoxyglycylglycylglycine [9]. Yield 1.6 g or 50% of the theoretical.

SUMMARY

A. Ya. Danilevsky's proposed structural links between amino acids, resulting in formation of an anhydride bond at their carboxyl groups, have been adequately confirmed by Frenkel's investigations as being possible structural fragments of protein.

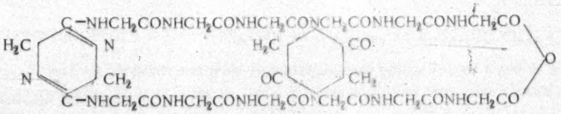
These investigations and ideas were undeservedly forgotten by later investigators in the protein field. We are compelled to conclude, however, that such forms of bond can be present in the protein molecule: 1) in the form of ester bonds (ester bonds of silk [10]), completely linking the organized molecules with one another; 2) as links between the final carboxyls of the tripeptides in monomer No. 1 or monomer No. 2:

No. 1

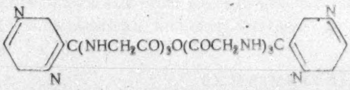


or

No. 2


C–NHCH₂CONHCH₂CONHCH₂CONCH₂CONHCH₂CONHCH₂CO
H₂C
N
H₂C
CO
O
N
CH₂
OC
CH₂
C–NHCH₂CONHCH₂CONHCH₂CO CH₂CONHCH₂CONHCH₂CO

3) as linear links between 2 monomers at the carboxyls



In the present investigation we succeeded in establishing the mechanism of synthesis of simple anhydrides from mixed anhydrides. We also studied the reaction of formation of N-aminoacyl derivatives of diketopiperazine with the help of simple anhydrides, and we made use of the latter in the preparation of peptides.

The following compounds were synthesized for the first time: 1) phthaloylglycine anhydride; 2) phthaloylglycine-chlorooxalyl anhydride; 3) carbobenzoxyalanine anhydride; 4) carbobenzoxyglycylglycine anhydride. The possibility was also demonstrated of formation by the same method of more complex peptide anhydrides (carbobenzoxyglycylglycylglycylglycine anhydride).

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ORGANIC INSECTOFUNGICIDES

XII. SYNTHESIS OF MIXED ESTERS OF PHOSPHORIC AND THIOPHOSPHORIC ACID

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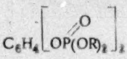
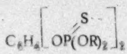
Several esters of phosphoric and thiophosphoric acids have found quite extensive application in agriculture as destroyers of various plant pests [1-14]. Diethyl-4-nitrophenylthiophosphate has found particularly extensive application, its destructive action considerably surpassing that of such active substances as DDT, hexachlorocyclohexane, nicotine and anabasine. This group of compounds has consequently attracted the interest of many investigators and at the present time several hundred derivatives of phosphoric and thiophosphoric acid have been studied for their action on plant pests; the number of compounds synthesized and studied in this field continually increases. But notwithstanding the great number of publications in this field there is an absence from the literature of systematic studies of the dependence of the activity of organic compounds of phosphorus in relation to plant pests on their structure.

In view of the great interest in this group of compounds, we undertook an investigation of the synthesis of various esters of phosphoric and thiophosphoric acids with the aim of studying the relation between the intensity of their action on plant pests and their structure.

In the first place we synthesized and studied the esters of phosphoric and thiophosphoric acids with the general formulas (I) and (II):

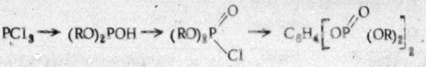


$C_6H_4[OP(=O)(OR)_2]_2$ (I)



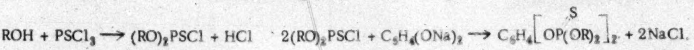
$C_6H_4[OP(=S)(OR)_2]_2$ (II)

Esters of phosphoric acid were synthesized by the general reaction applied to the preparation of compounds of this type [15]:



$$PCl_3 \rightarrow (RO)_2POH \rightarrow (RO)_2P(=O)Cl \rightarrow C_6H_4[OP(=O)(OR)_2]_2$$

Mixed esters of thiophosphoric acid were similarly prepared according to the following general schemes [16, 17]:



$$ROH + PSCl_3 \rightarrow (RO)_2PSCl + HCl \quad 2(RO)_2PSCl + C_6H_4(ONa)_2 \rightarrow C_6H_4[OP(=S)(OR)_2]_2 + 2NaCl$$

The compounds that we prepared and their properties are set out in Tables 1 and 2, and their activity toward the grain weevil (Calandra granaria) is detailed in Table 3. The pesticidal tests were carried out by P.V. Popov.

From the data of Table 3 we see that the phosphoric acid esters are more active than the thiophosphoric acid esters. The activity of phosphoric acid esters increases with increasing molecular weight of the aliphatic hydrocarbon radical, while that of the thiophosphoric acid esters decreases. Hydroquinone derivatives are rather more active than resorcinol derivatives.

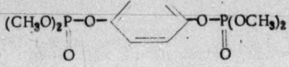
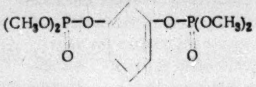
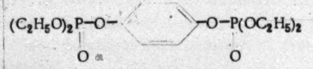
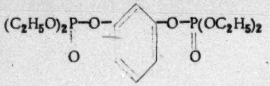
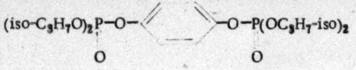
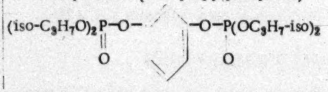
EXPERIMENTAL

Preparation of mixed esters of phosphoric acid. Into a flask fitted with a reflux condenser and a stirrer we introduced 1 mole of the phenol, 2 moles dialkylchlorophosphate, 4-8 times the weight of acetone and 2.3 moles anhydrous sodium carbonate in fine powder form. The mixture was boiled with thorough stirring for 4-6 hours. At the conclusion of the reaction the formed NaCl, $NaHCO_3$ and the excess of sodium carbonate were filtered off, the acetone was distilled off from the filtrate and the residue was fractionated in vacuum. The compounds so prepared are listed in Table 1. Phosphorous determinations on all the compounds were carried out by the photocolorimetric method.

Preparation of mixed esters of thiophosphoric acid. We employed Toy's [18] method in slightly modified form. Into a four-necked flask fitted with a stirrer, dropping funnel, thermometer and reflux condenser was introduced the phenol to which had been added an equimolecular amount of sodium methylate. The methyl alcohol was distilled off and to the dry residue was added chlorobenzene and the appropriate dialkylchlorothiophosphate.

TABLE 1

Properties of Phosphoric Acid Esters

Prep. No.	Name and formula	B.p.	d_4^{20}	n_D^{20}	Yield (%)	Analysis for P (%)	
						found	calc.
1	1,4-Phenylenebis-(dimethylphosphate) 	95-98° at 0.02 mm	1.3883	1.4738	70	18.65, 18.72	19.02
2	1,3-Phenylenebis-(dimethylphosphate) 	110-115 at 0.025 mm	1.2720	1.4997	31	18.75, 18.82	19.02
3	1,4-Phenylenebis-(diethylphosphate) 	118-121 at 0.15 mm	1.1913	1.4575	61	15.95, 16.32	16.02
4	1,3-Phenylenebis-(diethylphosphate) 	155-156 at 0.13 mm	1.2048	1.4856	39	15.87, 15.93	16.02
5	1,4-Phenylenebis-(diisopropylphosphate) 	102-110 at 0.024 mm	1.2250	1.4440	78.5	14.01, 13.97	14.15
6	1,3-Phenylenebis-(diisopropylphosphate) 	110-112 at 0.035 mm	1.1069	1.4500	78.7	13.8, 13.98	14.15

A few drops of pyridine were added as catalyst and the reaction mixture was heated with good stirring to 120-130° for 7-15 hours. At the end of the reaction the separate sodium chloride was filtered off. The chlorobenzene was distilled off from the filtrate in vacuum and the residue was washed with water, dried with calcium chloride and distilled in vacuum. The compounds that we prepared and their properties are presented in Table 2.

SUMMARY

1. 12 mixed esters of phosphoric and thiophosphoric acids were synthesized.

2. An examination of the activity of the synthesized esters toward the grain weevil showed that phosphoric acid esters are more active than thiophosphoric acid esters. Hydroquinone derivatives are more active than resorcinol derivatives.

The activity of phosphoric acid esters rises with increasing molecular weight of the aliphatic hydrocarbon radical. All the synthesized esters were less active than diethyl-4-nitrophenylthiophosphate.

TABLE 2

Properties of Thiophosphoric Acid Esters

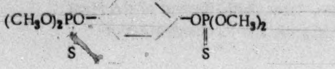
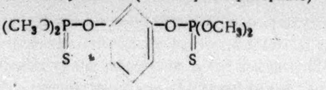
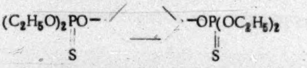
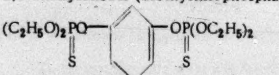
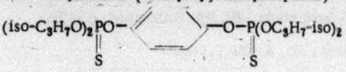
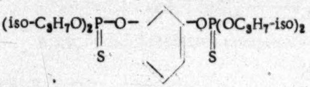
Prep. No.	Name and formula	B.p.	d_4^{20}	n_D^{20}	Yield (%)	Analysis for P (%)	
						found	calc.
1	1,4-Phenylenebis-(dimethylthiophosphate) 	105° at 0.04 mm	1.2428	1.5230	29	17.1, 17.0	17.32
2	1,3-Phenylenebis-(dimethylthiophosphate) 	120-125 at 0.16 mm	1.2890	1.5310	71	17.00, 16.95	17.32
3	1,4-Phenylenebis-(diethylthiophosphate) 	134 at 0.2 mm	1.2496	1.5158	28	14.72, 14.74	14.95
4	1,3-Phenylenebis-(diethylthiophosphate) 	130 at 0.15 mm	1.1991	1.5113	51.5	14.63, 14.69	14.95
5	1,4-Phenylenebis-(diisopropylthiophosphate) 	Does not distil at 0.05 mm without decomp.	1.1720	1.5193	58.0	13.4, 13.32	13.2
6	1,3-Phenylenebis-(diisopropylthiophosphate) 	Ditto	1.1352	1.5103	33.4	12.95, 13.06	13.2

TABLE 3

Activity of Esters of Phosphoric and Thiophosphoric Acids toward the Grain Weevil.

Prep. No.	Name	Maximum concentration of preparation giving 100% kill of grain weevil in 24 hours multiplied by 10^3 (in %)
1	1,4-Phenylenebis-(dimethylphosphate)	50-100
2	1,3-Phenylenebis-(dimethylphosphate)	Over 100
3	1,4-Phenylenebis-(diethylphosphate)	25-50
4	1,3-Phenylenebis-(diethylphosphate)	Over 100
5	1,4-Phenylenebis-(diisopropylphosphate)	5-25
6	1,3-Phenylenebis-(diisopropylphosphate)	5-25
7	1,4-Phenylenebis-(dimethylthiophosphate)	100-250
8	1,3-Phenylenebis-(dimethylthiophosphate)	Over 1000
9	1,4-Phenylenebis-(diethylthiophosphate)	" 1000
10	1,3-Phenylenebis-(diethylthiophosphate)	" 100
11	1,4-Phenylenebis-(diisopropylthiophosphate)	" 1000
12	1,3-Phenylenebis-(diisopropylthiophosphate)	" 1000
13	Diethyl-4-nitrophenylthiophosphate	2.5-5

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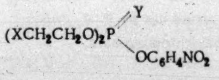
ORGANIC INSECTOFUNGICIDES

XIII. SYNTHESIS OF MIXED ESTERS OF PHOSPHORIC AND THIOPHOSPHORIC ACIDS CONTAINING THE SIMPLEST SUBSTITUENTS IN THE ALIPHATIC RADICAL

M. L. Galashina, I. L. Vladimirova, Ya. A. Mandelbaum and N. N. Melnikov

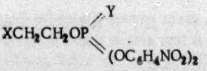
It was recently shown [1] that dialkynitrophenylthiophosphates are fairly active insecticides, while diethyl-4-nitrophenylthiophosphate has found practical application in agriculture [2-10]. We also know that the position and character of the substituent in the aromatic radical very profoundly influence the insecticidal activity of a compound. In this connection it was of interest to synthesize and study mixed esters of phosphoric and thiophosphoric acids containing the simplest possible substituents in the aliphatic radical and a nitrogroup in the aromatic radical.

In the first instance we synthesized compounds with the general formulas (I) and (II):



$$(XCH_2CH_2O)_2P(=Y)OC_6H_4NO_2$$

(I)

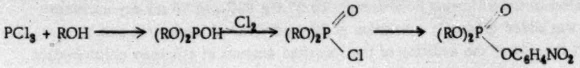


$$XCH_2CH_2OP(=Y)(OC_6H_4NO_2)_2$$

(II)

where X is chlorine or C_2H_5O and Y is oxygen or sulfur.

These compounds were synthesized by the general reaction for this type of compound.



$$PCl_3 + ROH \longrightarrow (RO)_2POH \xrightarrow{Cl_2} (RO)_2P(=O)Cl \longrightarrow (RO)_2P(=O)OC_6H_4NO_2$$

$$ROH + PSCl_3 \longrightarrow ROPSCl_2 \longrightarrow ROPS(OC_6H_4NO_2)_2;$$

$$ROH + PSCl_3 \longrightarrow (RO)_2PSCl \longrightarrow (RO)_2PSOC_6H_4NO_2.$$

A list of the synthesized compounds and their properties appears in Table 1.

TABLE 1

Name and formula	M.p.	d_4^{20}	n_D^{20}	Analysis for P (%)	
				found	calculated
β-Chloroethyl-4,4'-dinitrodiphenylphosphate $ClCH_2CH_2OPO(OC_6H_4NO_2)_2$	86-87°	–	–	7.24, 7.46	7.70
β-Chloroethyl-4,4'-dinitrodiphenylthiophosphate $ClCH_2CH_2OPS(OC_6H_4NO_2)_2$	95-96	–	–	7.50, 7.60	7.40
β,β'-Dichloroethyl-4-nitrophenylthiophosphate $(ClCH_2CH_2O)_2PSOC_6H_4NO_2$	Does not distil at 0.02 mm	–	1.5780	8.00, 8.21	8.61
β-Ethoxyethyl-4'-dinitrodiphenylphosphate $C_2H_5OCH_2CH_2OPO(OC_6H_4NO_2)_2$	72-73	–	–	7.50, 7.42	7.53
β-Ethoxyethyl-4,4'-dinitrodiphenylthiophosphate $C_2H_5OCH_2CH_2OPS(OC_6H_4NO_2)_2$	75-76	–	–	7.3, 7.22	7.23
β,β'-Diethoxydiethyl-4-nitrophenylphosphate $(C_2H_5OCH_2CH_2O)_2PO(OC_6H_4NO_2)$	–	1.2720	1.5050	8.32, 8.20	8.5

TABLE 2

Name and formula	M.p.	d_4^{20}	n_D^{20}	Analysis for P (%)		Yield (%)
				found	calculated	
β-Chloroethyldichlorothiophosphate $ClCH_2CH_2OPSCl_2$	104-108° at 14 mm	1.4671	1.5362	14.65, 14.71	14.52	44
β,β'-Dichlorodiethylchlorothiophosphate $(ClCH_2CH_2O)_2PSCl$	130 at 17 mm	1.5135	1.5641	11.85, 11.78	12.05	24
β,β',β''-Trichlorotriethylthiophosphate $(ClCH_2CH_2O)_3PS$	142-150 at 9 mm	1.4778	1.5650	10.12, 10.10	10.20	30
β-Ethoxyethyldichlorothiophosphate $C_2H_5OCH_2CH_2OPSCl_2$	108-114 at 23 mm	1.294	1.4910	13.4, 13.3	13.68	32
β-Ethoxyethyldichlorophosphate $C_2H_5OCH_2CH_2OPOCl_2$	110-114 at 21 mm	1.317	1.4452	14.5, 14.8	14.96	44
β,β'-Diethoxydiethylchlorophosphate $(C_2H_5OCH_2CH_2O)_2POCl$	154 at 7 mm	1.152	1.4310	11.52, 11.63	11.8	85

Tests of the synthesized compounds on the grain weevil (Calandra Granaria), carried out by P. V. Popov, showed that the whole of this group of compounds is less active than diethyl-4-nitrophenylthiophosphate.

EXPERIMENTAL

1. Preparation of alkylchlorothiophosphates. We prepared alkylchlorothiophosphates by reacting the appropriate alcohol with thiophosphorylchloride in presence of pyridine [11]. For example, β,β'-dichlorodiethylchlorothiophosphate was prepared in the following conditions: To 37.6 g $PSCl_3$ in 70 ml dry dichloroethane at −2° and with good stirring was added gradually a solution of 32 g ethylene chlorohydrin and 32 g pyridine in 32 ml dichloroethane. At the end of the addition of the specified amount of ethylene chlorohydrin and pyridine, the reaction mixture was stirred for 3 hours at 5-10°. Later the reaction mixture was treated with ice water for removal of pyridine hydrochloride. The dichloroethane solution was dried with sodium sulfate and after distillation of the dichloroethane (in vacuum) the residue was distilled in vacuum. Yield 9 g (24%).

Other esters of chlorothiophosphoric acid were similarly prepared. The properties of the prepared compounds are presented in Table 2. Esters of dichlorophosphoric acid were prepared by reaction of the corresponding alcohol with phosphorus oxychloride.

2. Preparation of mixed esters of phosphoric and thiophosphoric acids. Mixed esters of thiophosphoric acid were synthesized by a slightly modified Toy procedure [12], involving reaction of esters of chlorothiophosphoric acid with dry p-nitrophenylphenate in chlorobenzene solution with pyridine as catalyst. Into a flask fitted with a stirrer, a reflux condenser and a thermometer was introduced the phenol to which was added an equimolar amount of sodium methylate. The methyl alcohol was evaporated off and to the dry residue was added chlorobenzene, the dialkylchlorothiophosphate and pyridine. The reaction mixture was kept at 130° for 5-7 hours. While cooling, the sodium chloride was filtered off; the chlorobenzene was distilled off in vacuum, and the residue was washed with water, dried and fractionated in vacuum. The compounds that we prepared are listed in Table 1. Of these compounds, only β,β'-dichlorodiethyl-4-nitrophenylthiophosphate has been described in a U.S. patent [13], while the others have not been described in the literature. The ester described in the U.S. patent had been prepared by an entirely different method.

SUMMARY

A series of mixed esters of phosphoric and thiophosphoric acids containing chlorine and ethoxyl in the aliphatic radical were synthesized and their properties examined. Of the compounds synthesized, not one exhibited greater activity as an insecticide than diethyl-4-nitrophenylthiophosphate.

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FREE RADICALS IN THE DECOMPOSITION REACTIONS OF BENZYLAMINODIAZOBENZENE IN SOLVENTS

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Very great interest has been aroused in recent years by azo and diazo compounds which decompose by a radical mechanism at relatively low temperatures [1]. Thus the azodinitriles and esters of azodicarboyxlic acids have been closely studied.

These compounds are good initiators of polymerization processes and possess a number of advantages over other agents in use for technical purposes, e.g. peroxides [2].

It is known that diazoaminobenzene can also be used as an initiator of polymerization of some vinyl derivatives, for example acrylonitrile in block form and butadiene in aqueous emulsion [3]. It acts as a slower (relative to benzoyl peroxide) but more continuous source of free radicals.

The mechanism of decomposition of azo compounds of the type of azodinitriles and esters of azodicarboxylic acids has been analyzed in the literature, but no data have been published about diazoamines. We therefore considered it of interest to study this process with reference to benzylaminodiazobenzene (I).

In the literature [4] this compound is described a yellow crystalline substance with m.p. 73°; capable of rearrangement to the tautomeric form (II) in presence of acids:

$$C_6H_5CH_2NH{-}N{=}N{-}C_6H_5 \rightleftarrows C_6H_5CH_2N{=}N{-}NHC_6H_5.$$

Our investigations revealed that this compound is less stable than diazoaminobenzene. Thermal decomposition of the dry substance starts at 95° and is accompanied by steady evolution of gas (the yield of nitrogen is 91.5% calculated on the number of evolved nitrogen molecules). In solvents (benzene, ethylene glycol monoethyl ether) vigorous decomposition starts at as low as 40-50° (nitrogen yield 90%). We refrained from attempting to purify the compound by recrystallization (due to its instability), but we usually treated its acetone solution with animal charcoal, filtered, and precipitated the benzylaminodiazobenzene with water. After cautious drying the substance melted at 72-74°.

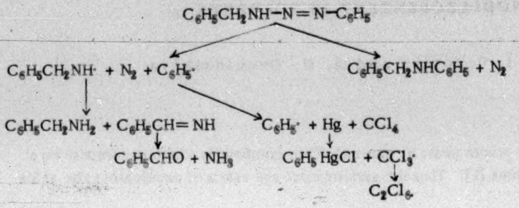
On the basis of the quantitative yield of nitrogen evolved during decomposition in solvents, it was suggested that decomposition of this compound can proceed in two directions: by a radical mechanism with formation of phenyl and benzylamino radicals and by an intramolecular mechanism with formation of benzylaniline.

We succeeded in establishing that both these processes take place probably simultaneously. It is true that neither of them can yet be accurately characterized, due to the difficulty of quantitative separation of the reaction products. The presence of benzylaniline could be demonstrated in all cases without particular difficulty. For the identification of the phenyl radical we made use of the method of fixation on mercury, frequently used in our laboratory.

For example, Razuvaev [5] established the release of the phenyl radical from benzoyl peroxide in carbon tetrachloride through the formation of phenyl mercury chloride. Again, Razuvaev and Fedotova [6] succeeded in binding the phenyl radical to mercury when benzeneazotriphenylmethane decomposed in carbon tetrachloride.

When benzylaminodiazobenzene was decomposed in similar conditions (in carbon tetrachloride in presence of mercury) a considerable amount of phenylmercury chloride could be isolated from the reaction mixture, thereby convincingly demonstrating the formation of the phenyl radical. The participation in this process of the solvent – carbon tetrachloride – was also confirmed by the isolation of hexachloroethane from the reaction mixture.

Benzaldehyde and benzylamine were detected in considerable amounts among the products of decomposition of benzylaminodiazobenzene in carbon tetrachloride in presence of mercury, as well as in ethylene glycol monoethyl ether. It is highly probable that the formation of these substances is associated with the benzylamino radical which by disproportionation is transformed into benzylamine and benzylimine. In the process of separation of the latter, it is hydrolyzed to benzaldehyde. Consequently the breakdown of benzylaminodiazobenzene in carbon tetrachloride in presence of mercury may be represented by the following probable scheme:


$C_6H_5CH_2NH-N=N-C_6H_5$
$C_6H_5CH_2NH\cdot + N_2 + C_6H_5\cdot$
$C_6H_5CH_2NHC_6H_5 + N_2$
$C_6H_5CH_2NH_2 + C_6H_5CH=NH$
$C_6H_5\cdot + Hg + CCl_4$
$C_6H_5CHO + NH_3$
$C_6H_5HgCl + CCl_3\cdot$
C_2Cl_6

Radical decomposition of benzylaminodiazobenzene in solvents was indirectly confirmed by the formation of acetaldehyde (in ethylene glycol monoethyl ether) due to splitting-off by the phenyl radical of hydrogen from the solvent (benzene could not be identified), as well as by formation of small amounts of diphenyl in exploratory experiments in benzene.

EXPERIMENTAL

1. Decomposition of Benzylaminodiazobenzene in Carbon Tetrachloride in Presence of Mercury

A solution of 6.6 g benzylaminodiazobenzene in 25 ml carbon tetrachloride in presence of 50 g metallic mercury was heated on a water bath with vigorous stirring for 7 hours. Completion of the reaction was signalized by cessation of evolution of nitrogen. The contents of the reaction flask were carefully decanted from the mercury, acidified with hydrochloric acid (for binding of amines) and steam-distilled. Carbon tetrachloride collected in the receiver together with a small amount of oily liquid with the characteristic odor of benzaldehyde. The carbon tetrachloride was separated from the aqueous layer, dried and distilled. Hexachloroethane crystallized from the residue. It was separated from the small amount of liquid fraction. Its weight was 0.5 g (7% of theory); m.p. 186° in a sealed capillary; m.p. of its mixture with a pure specimen in a sealed capillary was 186°. After separation of the crystals of hexachloroethane, the liquid was combined with the ether extracts from the aqueous layer and fractionated. A fraction boiling at 176-182° was isolated in the amount of 1.2 g (34.3% of theory) and tested for the presence of the carbonyl group. The following were prepared:

Dimedone derivative with m.p. 196° (according to the literature the dimedone derivative of benzaldehyde melts at 195°). A mixture with a pure specimen melts at 195°. 2,4-Dinitrophenylhydrazone with m.p. 235° (237° in the literature); a mixture with a pure sample melts at 237°. A silver mirror was formed with ammoniacal mercuric oxide. The presence of benzaldehyde was thus definitely confirmed.

After distilling off the carbon tetrachloride and the benzaldehyde, the liquid remaining in the flask was made alkaline and again steam-distilled. At the end of the distillation, the flask contained a resinous residue (A). The condensate was extracted with ether, dried and fractionated to give a benzylamine fraction of 0.5 g, boiling at 182° (yield 15% of theory) and a benzylaniline fraction of 1.3 g (19.5%) boiling at 302°. The benzylamine was identified by formation of benzylphthalimide with m.p. 115° (literature 116°) (a mixed sample melts at 115°) and by formation of a crystalline derivative with ethyl acetate melting at 60° (literature 61°; mixed m.p. 60°). Benzylaniline was identified as the nitrosamine by Liebermann's reaction [7] and from the m.p. of the hydrochloride (222° compared with the literature value of 224°). The molecular weight of the salt was determined by titration with alkali in presence of phenolphthalein. Found: M 222.6. $C_{13}H_{14}Cl$. Calculated: M 219.5.

The mercury and the resinous substance (A) were repeatedly treated with hot acetone. After cooling, the acetone deposited crystals of phenylmercuric chloride in the amount of 1.5 g with m.p. 256° (literature 258°; mixed m.p. 257°). The yield of phenylmercuric chloride is 15.7% of theory.

2. Decomposition of Benzylaminodiazobenzene in Ethylene Glycol Monoethyl Ether

A solution of 2.5 g benzylamino diazobenzene in 20 ml ethylene glycol monoethyl ether was heated first on the water bath and then on a metal bath until nitrogen ceased to come off. The reaction mixture was acidified and steam-distilled. The condensate was extracted with ether, the ether extract was dried and fractionated.

Fractionation gave 0.35 g benzaldehyde (31.5% of theory). From this fraction was prepared the dimedone derivative of benzaldehyde with m.p. 196°, also the 2,4-dinitrophenylhydrazone with m.p. 235°. The residue in the reaction flask was made alkaline and again steam-distilled. The condensate was extracted with ether, the ether extract was dried and the ether driven off. The benzylamine in the residue was separated from the benzylaniline by treatment with phthalic anhydride. 0.23 g benzylphthalimide with m.p. 115° (literature 116°) was isolated. On the basis of benzylamine the yield was 0.1 g (10% of theory). 0.5 g (20% of theory) benzylaniline was isolated and identified in the form of the nitrosamine by Liebermann's reaction and by the m.p. of the hydrochloride (220°). In the aqueous solution, after steam distillation, was found acetaldehyde, identified as the dimedone derivative with m.p. 140° (literature 140°; mixture with the pure substance melts at 140°), and as the 2,4-dinitrophenylhydrazone with m.p. 160-168° (literature 168°). The mixed melting point was 167°. The acetaldehyde was not quantitatively determined. Benzene could not be detected among the reaction products.

SUMMARY

1. The decomposition of benzylaminodiazobenzene in ethylene glycol monoethyl ether and carbon tetrachloride in presence of mercury was studied. Benzaldehyde, benzylamine, benzylaniline and acetaldehyde were separated from the products of reaction in ethylene glycol monoethyl ether. Phenylmercuric chloride, benzaldehyde, benzylamine and benzylaniline were separated from the products of reaction in carbon tetrachloride.

2. The composition of the reaction products indicated that two processes proceed simultaneously — a radical process (with formation of phenyl and benzylamino radicals) and an intramolecular process (with formation of the secondary amine, benzylaniline).

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* See Consultants Bureau translation, p. 1219.

THE PROBLEM OF THE MECHANISM OF FORMATION OF 2-SUBSTITUTED OXAZOLONES

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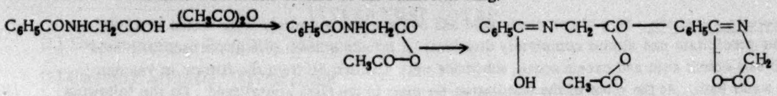
It is known that 2-phenyl-5-oxazolone is readily formed by reaction of hippuric acid with acetic anhydride [1]. The yield of oxazolone can be raised from 49 to 64% by treating hippuric acid with a large excess of acetic anhydride at 15-20°.

All attempts to prepare 2-benzyl-5-oxazolone from phenaceturic acid have proved unsuccessful. Many investigators [2] have tried to demonstrate its presence in the reaction mass by preparing derivatives; for example, treatment with ammonia and benzylamine gave the amide and benzylamide of phenaceturic acid; this method, however, cannot serve as evidence of the formation of 2-benzyl-5-oxazolone. Indeed, the action on phenaceturic acid of various dehydrating agents such as acetic anhydride, phosphorus tribromide, etc. may be expected to lead to formation of the mixed anhydride of phenaceturic and acetic acids or the anhydride of phenaceturic acid. When these compounds are treated with ammonia or benzylamine they will give the same substances as are formed by 2-benzyl-5-oxazolone.

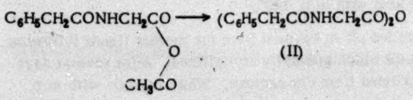
In this investigation an attempt has been made to study the mechanism of the reaction between phenaceturic acid and acetic anhydride and to ascertain why 2-benzyl-5-oxazolone is not formed.

In all probability the process of formation of 2-phenyl-5-oxazolone from hippuric acid and acetic anhydride proceeds through the stage of the mixed anhydride of hippuric and acetic acids with simultaneous tautomerization of the amido bond and closure of the oxazolone ring.


$C_6H_5CONHCH_2COOH \xrightarrow{(CH_3CO)_2O} C_6H_5CONHCH_2CO$
$CH_3CO—O$
$C_6H_5C=N-CH_2-CO$
OH
CH_3-CO
O
$C_6H_5C=N$
CH_2
O-CO

The susceptibility of the amido bond to tautomeric transformation is an indispensable condition for formation of the oxazolone ring. It is very probable that different acylamino acids differ from one another in susceptibility to tautomeric change of the amido bond and that they are capable to a greater or lesser extent of changing into oxazolones in dependence on the structure of the amino acid and of the acylating carboxylic acid. We know that not only hippuric acid but also many of its derivatives readily change into oxazolones [3]. When the tautomerism of the acylamino acids is weakly developed, the oxazolone is formed in such small amount that it does not appear possible to isolate it in the pure form.

Phenaceturic acid may be regarded as belonging to this type of acylamino acids. When reacted with acetic anhydride, it apparently first forms the mixed anhydride of phenaceturic and acetic acids (I), which dissolves in excess acetic anhydride. In the course of removal of the acetic anhydride, the equilibrium is shifted in the direction of formation of phenaceturic anhydride (II) which quickly crystallizes at the conclusion of the distillation:


$C_6H_5CH_2CONHCH_2CO \longrightarrow (C_6H_5CH_2CONHCH_2CO)_2O$
O
CH_3CO

(I) (II)

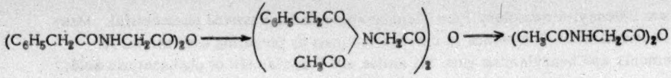
Compound (II) usually contains a small amount of the anhydride of N-acetylphenaceturic acid which is removed by recrystallization from acetone.

After filtration of phenaceturic anhydride, the mother liquor is concentrated in vacuum and left to crystallize. After a few days the anhydride of N-acetylphenaceturic acid comes down. The non-susceptibility to tautomerism of the amide bond in phenaceturic anhydride prevents it from undergoing transformation into 2-benzyl-5-oxazolone. Phenaceturic anhydride very readily enters into reaction with acetic anhydride, forming N-acetylphenaceturic anhydride. The reaction takes place even in the cold, and this may be accounted for by the great lability of the hydrogen of the amido group.

Under the action of ammonia, N-acetylphenaceturic anhydride breaks down to phenylacetamide, the amide of aceturic acid, and aceturic acid (the latter was not isolated from the mother liquors). The action of sodium hydroxide solution on N-acetylphenaceturic acid leads to salts of aceturic and phenylacetic acids.

The above reactions justify the assumption that the phenacetyl residue in N-acetylphenaceturic acid is less firmly attached to the amido group than is the acetyl residue.

In the preparation of various oxazolones by Erlenmeyer's method from phenaceturic, caproylaminoacetic and other acids, transacylation readily occurs of the acylamino acids [4]. On the basis of the foregoing facts, it follows that the transacylation reaction proceeds through the stage of formation of intermediate mixed diacylamino acids which in the course of further reaction readily lose one acylating group.



$$(C_6H_5CH_2CONHCH_2CO)_2O \longrightarrow \left(\begin{matrix} C_6H_5CH_2CO \\ CH_3CO \end{matrix} \Big\rangle NCH_2CO \right)_2 O \longrightarrow (CH_3CONHCH_2CO)_2O$$

Hippuric acid evidently readily gives the tautomeric form of the amido bond and is therefore incapable of forming diacylamino acids but is at once converted into 2-phenyl-5-oxazolone.

EXPERIMENTAL

2-Phenyl-5-oxazolone. 30 g hippuric acid was mixed with 350 g acetic anhydride at 20° for 8 hours. The residual hippuric acid (13.6 g) was filtered off and dried.

The filtrate was concentrated on a water bath at 40° in vacuum. The residual orange oil crystallized. The azlactone was extracted from this mass with petroleum ether three times (100 ml each time) at 60-70°. Cooling of the solution to 0° led to separation of large, lustrous, orange plates. Yield 12 g or 64%. The azlactone was recrystallized from absolute ethyl alcohol (1:3). Yellow plates with m.p. 90-92° (I).

Phenaceturic anhydride. 30 g phenaceturic acid and 300 g acetic anhydride were mixed at 15-20° for 4 hours until the precipitate had almost completely dissolved. A minute amount (0.5 g) phenaceturic acid was filtered off and acetic acid and excess acetic anhydride were distilled off from the filtrate in vacuum at 40-45° on a water bath. At the close of the distillation the mass in the flask crystallized. On the following day the crystal mass was well stirred with 100 ml absolute ether and the insoluble white crystalline material was filtered off, washed with absolute ether and recrystallized from dry acetone. White, finely crystalline precipitate with m.p. 108-109°. Yield 17 g.

3.740 mg substance: 8.841 mg CO_2; 1.815 mg H_2O. 3.737 mg substance: 8.871 mg CO_2; 1.919 mg H_2O.
5.104 mg substance: 0.338 ml N_2 (21°, 732 mm); 5.670 mg substance: 0.374 ml N_2 (21°, 732 mm).
0.1768 g substance: 2.05 ml 0.5 N NaOH (back titration) 0.2510 g substance: 2.9 ml 0.5 N NaOH.
Found %: C 64.51, 64.78; H 5.43, 5.74; N 7.4, 7.37; Anhydride groups; 20.87, 20.79. $C_{20}H_{20}O_5N_2$.
Calculated %: C 65.16; H 5.48; N 7.60; anhydride groups 19.57.

Heat was developed when 1 g of the substance was dissolved in 10 ml concentrated ammonia and on the following day a precipitate of the amide of phenaceturic acid came down with m.p. 174-175°.

Hydrolysis of 1 g anhydride with 10 ml 5% sodium hydroxide solution followed by acidification with hydrochloric acid solution led to separation of phenaceturic acid with m.p. 143°.

N-Acetylphenaceturic anhydride. The ether was distilled off in vacuum from the mother liquor following filtration of phenaceturic anhydride, leaving a thick, brown oil which gradually crystallized. After several days the crystals were filtered, washed with dry ether and recrystallized from dry acetone. White crystals with m.p. 175-176°.

6.870 mg substance: 0.372 ml N_2 (22°, 736 mm). 6.783 mg substance: 0.357 ml N_2 (20.5°, 741 mm).
Found %: N 6.07, 5.99. $C_{24}H_{24}O_7N_2$. Calculated %: N 6.17.

Cleavage of N-acetylphenaceturic anhydride with aqueous ammonia. 4.5 g of the substance was treated with 50 ml ammonia; heat was developed. On the following day the precipitate was filtered and dried at 60°. M.p. 156° (after recrystallization from water). It was identified as the amide of phenylacetic acid by the absence of depression in the mixed melting point determination. Yield 2.4 g.

The solution after filtration of the phenylacetamide was evaporated to dryness in vacuum on a water bath. The crystalline residue was dissolved in 8 ml ethyl alcohol. Rapid separation occurred of large white prisms which were recrystallized from 5 ml alcohol. M.p. 135-137° [5].

3.521 mg substance: 5.379 mg CO_2; 2.250 mg H_2O. 4.001 mg substance: 6.090 mg CO_2; 2.440 mg H_2O. 6.772 mg substance: 11.8 ml 0.01 N H_2SO_4. 4.344 mg substance: 7.65 ml 0.01 N H_2SO_4 (Kjeldahl). Found %: C 41.69, 41.54; H 7.15, 6.82; N 24.4, 24.66. $C_4H_8O_2N_2$. Calculated %: C 41.36; H 6.94; N 24.12.

This compound was identified as aceturic acid amide.

Cleavage of N-acetylphenaceturic anhydride by sodium hydroxide solution. 6.3 g anhydride was mixed with 20 ml water and gradual addition was made of 13 ml 15% sodium hydroxide solution. The precipitate rapidly dissolved with development of heat. On the next day the solution was made neutral, treated with carbon, filtered and acidified with concentrated hydrochloric acid. Lustrous scaly crystals came down. These were filtered and recrystallized from water. M.p. 76°. They were identified by the absence of depression in the mixed m.p. determination with phenylacetic acid. Yield 2.8 g.

After separation of the phenylacetic acid, the filtrate was evaporated to dryness in vacuum on the water bath, and the resultant white crystalline mass was treated with 5 ml cold water. The insoluble portion was filtered off, washed with ether for removal of the phenylacetic acid and twice recrystallized from a little water. Dried at 100°, the compound melted at 207-208°. No m.p. depression with aceturic acid [6].

SUMMARY

Acetic anhydride reacts with phenaceturic acid to give phenaceturic anhydride and N-acetylphenaceturic anhydride. When treated with ammonia, the N-acetyl derivative breaks down to phenylacetamide and the amide of aceturic acid; hydrolysis with caustic alkali gives phenylacetic and aceturic acids.

It is suggested that the absence of tautomerism from the amido bond of phenylaceturic acid is the cause of its inability to form 2-benzyl-5-oxazolone.

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THIOSEMICARBAZONES OF BENZOPHENONE AND OF SOME OF ITS DERIVATIVES. II*

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Thiosemicarbazones of aldehydes have recently acquired great interest due to the antitubercular activity exhibited by some of them [1]. Regarding benzophenone as benzaldehyde in which the benzaldehydic hydrogen is replaced by the phenyl radical, it appeared to us of interest to prepare a series of thiosemicarbazones of benzophenone and its derivatives for assay of their tuberculostatic activity in comparison with the thiosemicarbazones of benzaldehyde and its derivatives. Consequently we prepared the thiosemicarbazones of the following compounds with the general formula $RC_6H_4COC_6H_4R_1$:

1) Benzophenone (R and R_1 = H); 2) p-methoxybenzophenone (R = H, R_1 = OCH_3); 3) p-hydroxybenzophenone (R = H, R_1 = OH); 4) p-nitrobenzophenone (R = H, R_1 = NO_2); 5) p-aminobenzophenone (R = H, R_1 = NH_2); 6) p-acetaminobenzophenone (R = H, R_1 = $NHCOCH_3$); 7) p,p'-dinitrobenzophenone (R and R_1 = NO_2); 8) p,p'-diaminobenzophenone (R and R_1 = NH_2).

The general method for their preparation consists in heating an alcoholic solution of the ketone with thiosemicarbazide, the alcohol being boiled for a period of 2-6 hours. It was sometimes necessary to add one to two drops of hydrochloric acid or to use thiosemicarbazide hydrochloride instead of the base. The use of such media, however, in presence of readily saponifiable N- and O-acetyl groups led to partial saponification of these groups and it was not possible to obtain the pure thiosemicarbazones from acetoxy-, p-diacetamino- and p,p'-diacetaminobenzophenone. In these cases we obtained a mixture of substances with a content of partially deacetylated products.

The Friedel-Crafts reaction was employed for the most part in the preparation of the initial p-substituted benzophenones.

The prepared thiosemicarbazones were examined by O. O. Makeeva of the chemotherapeutic department of our institute. It was established that their antitubercular activity in vitro was very insignificant in relation to that of thiosemicarbazones of aldehydes.

EXPERIMENTAL

1. Benzophenone was prepared by the Friedel-Crafts reaction by condensation of benzene with benzoyl chloride in presence of aluminum chloride. The thiosemicarbazone was prepared by adding 1 g finely pulverized thiosemicarbazide to 2 g of benzophenone dissolved in 25 ml alcohol. The mixture was heated at 80° with good stirring for 4 hours. After cooling, the solution deposited lustrous white crystals (2.5 g). They were washed with hot water and recrystallized from alcohol. M.p. 170-171°. Yield 2.3 g (82% of the theoretical). The substance is insoluble in water, slightly soluble in cold alcohol.

Found %: N 16.30; S 12.58. $C_{14}H_{13}N_3S$. Calculated %: N 16.47; S 12.55.

2. p-Methoxybenzophenone [2]. To a mixture of 40 g anisole, 56 g benzoyl chloride and 100 ml carbon bisulfide was gradually added, with stirring, 80 g aluminum chloride. 2 hours after the addition of the whole of the aluminum chloride, the reaction mass was warmed up to 40-45° for 2 hours and left overnight. The next morning the carbon bisulfide was distilled off in vacuum, the reaction mass was decomposed with ice water and extracted with ether; the ethereal solution was dried and distilled, and the residue distilled in vacuum (6 mm) at 184-187°. There was obtained 52 g (66%). The substance was dissolved in ether; slow removal of the solvent resulted in separation of large white crystals with m.p. 60-61°.

Methoxybenzophenone thiosemicarbazone was prepared similarly to benzophenone thiosemicarbazone. The obtained precipitate was washed with hot water and crystallized from 50% alcohol. Yield 60% of the theoretical. M.p. 183-184°.

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* Communication I see: Proceedings of the Mendeleev All-Union Chemical Society, 1953, No. 2.

Found %: N 14.67; S 11.24. $C_{15}H_{15}ON_3S$. Calculated %: N 14.73; S 11.22.

3. p-Hydroxybenzophenone [3] was prepared by demethylation of p-methoxybenzophenone by heating to boiling a solution of p-methoxybenzophenone in 5 times the amount of glacial acetic acid containing 48% HBr for 10 hours. The solution was poured into water, neutralized with sodium carbonate and extracted with ether; the ether was distilled off and the residue dissolved in 5% sodium hydroxide. The insoluble residue was filtered off and the solution was acidified with hydrochloric acid to bring down the p-hyrdroxybenzophenone. Yield 72% of the theoretical. M.p. 133-134°.

p-Hydroxybenzophenone thiosemicarbazone was prepared by boiling an alcoholic solution of p-hydroxybenzophenone and thiosemicarbazide for 4 hours. At the end of the reaction, after cooling the solution, a precipitate did not come down. The alcohol was distilled off, the residue washed with hot water (in which it partly dissolved) and crystallized from 50% alcohol. White crystals with m.p. 188-190° were obtained. The product is soluble in ether, acetone and hot alcohol, insoluble in benzene and water. Yield 65% of the theoretical.

Found %: S 11.65; N 15.43. $C_{14}H_{13}ON_3S$. Calculated %: S 11.80; N 15.50.

4. p-Nitrobenzophenone was prepared by condensing p-nitrobenzoyl chloride with benzene (3 times the quantity) in presence of aluminum chloride at room temperature. The reaction mass was left overnight and on the following day it was heated at 45-50° for 2 hours; it was thereupon decomposed with ice water and the benzene was distilled off with steam. The residue was filtered, washed with 2% sodium hydroxide solution and recrystallized from alcohol.

M.p. 135°. Yield 90% of the theoretical.

When p-nitrobenzophenone was boiled with thiosemicarbazide in alcohol for 6 to 10 hours, it was recovered unchanged. With the addition of one to two drops of hydrochloric acid, the reaction was performed for 3 hours. When the alcoholic solution was cooled, a precipitate came down and was washed with hot water and recrystallized from 80% alcohol. M.p. 205-206°. Yield 75% of the theoretical. The substance is readily soluble in chloroform, insoluble in water. It crystallizes from alcohol and aqueous alcohol.

Found %: N 18.88; S 10.60. $C_{14}H_{12}O_2N_4S$. Calculated %: N 18.66; S 10.66.

5. p-Aminobenzophenone is prepared by reducing p-nitrobenzophenone with molecular hydrogen in presence of Raney nickel while shaking in a medium of alcohol at normal pressure and room temperature. The theoretical amount of hydrogen was absorbed. The reaction mass was heated and filtered, the alcohol was distilled off in vacuum and the residue extracted with a hot solution of dilute hydrochloric acid (1:5). The solution was treated with carbon and filtered; the amine was fractionally separated by addition of ammonia to the cold filtrate. Crystallization from aqueous alcohol gave white crystals with m.p. 123-124°. Yield 58% of the theoretical.

p-Aminobenzophenone thiosemicarbazone was prepared by heating an alcoholic solution of p-aminobenzophenone with thiosemicarbazide in presence of a drop of concentrated hydrochloric acid for 3 hours. On cooling, an insignificant amount of thiosemicarbazide was precipitated and was filtered off. The alcoholic filtrate was distilled in vacuum and the residue was repeatedly washed with ether and recrystallized from 50% alcohol. M.p. 155-157°. Yield 30%. Soluble in alcohol and acetone, slightly soluble in water.

Found %: N 20.51; S 11.91. $C_{14}H_{14}N_4S$. Calculated %: N 20.74; S 11.85.

6. p-Acetaminobenzophenone was prepared by heating p-aminobenzophenone with acetic anhydride on a boiling water bath for 2 hours. The solution was poured into water and the precipitate was recrystallized from aqueous alcohol. M.p. 150-151°. Yield 95% of the theoretical.

p-Acetaminobenzophenone thiosemicarbazone was prepared by heating an alcoholic solution of p-acetaminobenzophenone with thiosemicarbazide for 4 hours. After cooling, a precipitate came down from the solution and was washed with hot water before recrystallization from aqueous alcohol. M.p. (with decomp.) 240-241° (rapid melting). Yield 73% of the theoretical.

Found %: N 17.77; S 10.23. $C_{16}H_{16}ON_4S$. Calculated %: N 17.94; S 10.25.

7. p-Diacetylaminobenzophenone. p-Aminobenzophenone was heated with acetic anhydride on a gauze at the boil for 3 hours. The mass was then poured into ice water and the precipitate was recrystallized from

aqueous alcohol. M.p. 172-173°. Yield nearly theoretical. Analysis showed that the substance was the diacetyl derivative of p-aminobenzophenone, not described in the literature.

Found %: N 5.04; CH_3CO 30.3; H 5.63; C 73.02. $C_{17}H_{15}O_3N$. Calculated %: N 4.98; CH_3CO 30.6; H 5.34; C 72.62.

The same compound is obtained if p-acetaminobenzophenone (m.p. 150-151°) is heated with acetic anhydride on a gauze for 2 hours. Saponification with hydrochloric acid in alcohol gave p-aminobenzophenone.

p-Diacetaminobenzophenone thiosemicarbazone could not be prepared in the pure form. When this reaction was performed in the usual conditions, crystallization from alcohol gave a substance with decomposition point 228-230°. Judging by the analyses for S and acetyl group, this was a mixture of the thiosemicarbazones of mono- and diacetaminobenzophenone. It was impossible to separate and purify the components. Apparently partial cleavage of the acetyl group occurs during the reaction.

8. p,p'-Dinitrobenzophenone was prepared by oxidizing 1,1-dichloro-p,p'-dinitrodiphenylethylene with chromic acid in glacial acetic acid. M.p. 188-189°.

When an alcoholic solution of p,p'-dinitrobenzophenone had been heated with thiosemicarbazide for 6-10 hours, the starting products were recovered unchanged. With the addition of one drop of hydrochloric acid, or by the use of thiosemicarbazide hydrochloride, dinitrobenzophenone thiosemicarbazone was obtained in quantitative yield after only 2 hours. The compound is insoluble in alcohol, soluble in hot acetone, and is precipitated from the latter on addition of water. Decomposition point 243.5-244°.

Found %: S 9.05. $C_{14}H_{11}O_4N_5S$. Calculated %: S 9.27.

9. p,p'-Diaminobenzophenone [4] was prepared by condensation of acetanilide with carbon tetrachloride in presence of freshly distilled aluminum chloride, followed by saponification of the resultant p,p'-diacetaminobenzophenone. Saponification of the acetyl groups with dilute sulfuric acid invariably gave a considerable amount of acid-insoluble precipitate. Saponification was preferably effected with a mixture of one part acetic acid and two parts hydrochloric acid (18%) by heating on the boiling water bath under a reflux condenser for 2 hours. After dilution of the reaction mass with ten times the amount of water followed by neutralization with ammonia until non-acid to Congo, a precipitate came down. It was crystallized from alcohol. M.p. 241-242° (with decomp.).

Heating of diaminobenzophenone with thiosemicarbazide in alcohol failed to yield the expected thiosemicarbazone. Successful preparation was prepared in the following conditions: To a suspension of 2 g p,p'-diaminobenzophenone in 60 ml alcohol was added a solution of 1.6 g thiosemicarbazide hydrochloride in 6 ml water. The mixture was left overnight at room temperature. The precipitate of diamine formed a red solution. The alcohol was distilled off in vacuum and the residue was dissolved in water. The solution was filtered and neutralized with 3% sodium bicarbonate solution to give a precipitate weighing 2.1 g and decomposing at 193-194°. Repeated crystallization from aqueous alcohol raised the decomp. pt. to 207-207.5°. The hydrochloride is soluble in water.

Found %: S 11.16. $C_{14}H_{15}N_5S$. Calculated %: S 11.23.

10. p,p'-Diacetaminobenzophenone was prepared pure by acetylation of diaminobenzophenone with acetic anhydride. M.p. 237°. Yield 85% of the theoretical.

Unsuccessful attempts were made to prepare p,p'-diacetaminobenzophenone thiosemicarbazone by heating with thiosemicarbazide in alcoholic solution or in alcohol containing hydrochloric or acetic acid, by heating in butyl alcohol or in alcohol containing thiosemicarbazide hydrochloride.

SUMMARY

1. 8 Thiosemicarbazones of benzophenone and its derivatives were prepared.

2. This reaction was shown to be catalyzed by hydrochloric acid in a number of cases.

3. Tests of the prepared compounds against tuberculosis organisms in vitro showed that the thiosemicarbazones of this series are either inactive towards the bacilli or possess an extremely weak activity.

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SYNTHESIS OF LEUCO BASES AND DYES OF THE TRIPHENYLMETHANE SERIES. II. [1]

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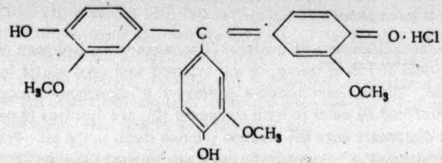
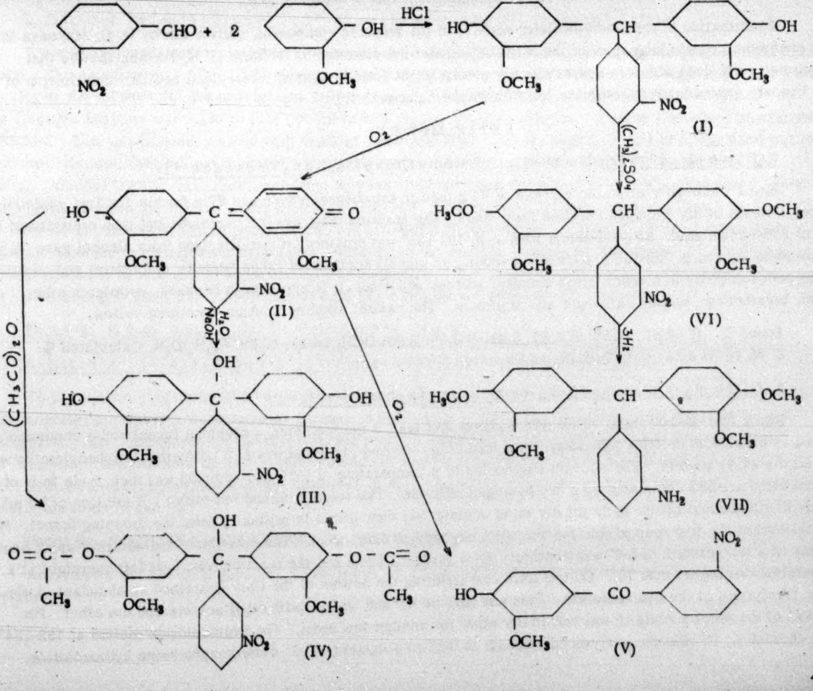
The preparation of rubrophen was disclosed in 1937 [2]. It is a dihydroxytrimethoxyfuchsone. Its hydrochloride is known to us by the name of rubrocol.



It proved to possess a very low toxicity and found application in the therapy of some nonpulmonaryforms of tuberculosis (tuberculosis of the glands [3,4], urinogenital tuberculosis [5], bone and joint tuberculosis). This prompted Soviet scientists to investigate compounds of the hydroxytriphenylmethane series [6,7], with the aim of finding more effective and more accessible agents for the cure of tuberculosis.

We have prepared compounds of the triphenylmethane series containing, in addition to hydroxy and methoxy groups, nitro, amino, sulfanilamino and other groups.

In this communication we describe 3-nitro-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane (I) and its transformation products. Starting materials for this synthesis were m-nitrobenzaldehyde and guaiacol. The research was carried out according to the following scheme:



Condensation of o-, m- and p-nitrobenzaldehydes with phenols and their ethers always gave amorphous, difficultly purifiable products which were characterized as pure substances on the basis of their analyses [8-11]. When the condensation of m-nitrobenzaldehyde with guaiacol was performed in a mixture of concentrated hydrochloric and glacial acetic acids, we obtained a crystalline substance in 90% yield which defied description; in analysis it corresponded to the product that we had expected to obtain – 3-nitro-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane (I). Examination showed, however, that it was heterogeneous; after its saturated acetic acid solution had stood for a lengthy period (about 2 months), separation occurred of up to 10% of a crystalline nitro compound with m.p. 138-140° whose analysis also corresponded to compound (I). Oxidation of the amorphous product gave up to 40% of 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone (II), likewise identical with the product of oxidation of the crystalline nitro compound (I). Furthermore, from the residual reaction mass was isolated a dye differing in properties from the compounds of the hydroxyfuchsone series (is not decolorized by caustic alkalies); we did not examine it more closely.

Condensation of m-nitrobenzaldehyde with guaiacol in presence of dry hydrogen chloride gas gave the crystalline compound (I) in a yield of 70% of theory. It was oxidized with amyl nitrite in ethyl acetate which contained dry hydrogen chloride. The resultant 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone crystallizes with molecular ether, is readily hydrolyzed by water to form compound (II), and dissolves in caustic alkali with a bright-blue color. The color disappears when the alkaline solution stands in the air. From the decolorized alkaline solution of 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone was isolated 3-nitro-4',4"-dihydroxy-3',3"-dimethoxytriphenylcarbinol (III). Acetylation of 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone (II) with acetic anhydride gave 3-nitro-4',4"-diacetoxy-3',3"-dimethoxytriphenylcarbinol (IV). Passage of a current of air through the alkaline solution of the nitrofuchsone (II) gave its cleavage product (not described in the literature), 3-nitro-4'-hydroxy-3'-methoxybenzophenone (V). The nitrofuchsone (II) possesses valuable properties as an indicator.

With the aim of establishing the necessity of the presence of free hydroxy groups for the tuberculostatic action of hydroxytriphenylmethane compounds, we methylated these groups in 3-nitro-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane. Methylation was performed with dimethyl sulfate in an alkaline medium. The obtained 3-nitro-4',4",3',3"-tetramethoxytriphenylmethane (VI) was reduced with hydrogen in presence of skeletal nickel catalyst to form 3-amino-4',4",3',3"-tetramethoxytriphenylmethane (VII).

Examination of the tuberculostatic activity of the prepared compounds, carried out by O. O. Makeeva in the chemotherapeutic laboratory of the VNIKhFI under the direction of Professor G. N. Pershin, showed that leuco bases and dyes with free hydroxy groups possess slight activity against tuberculosis bacilli. Substitution of the hydroxy groups leads to complete loss of antitubercular activity.

EXPERIMENTAL

3-Nitro-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane (I)

Into a thoroughly triturated mixture of 46 g pure m-nitrobenzaldehyde and 82 g freshly distilled guaiacol was passed a steam of dry hydrogen chloride for 4 hours. The reaction mass was left overnight and then crystallized from 90 ml 80% acetic acid. 85 g substance with m.p. 133-136° was obtained. Crystallization from alcohol gave 78 g of a substance with m.p. 138-140°. It dissolves readily in glacial acetic acid (when heated), chloroform and caustic alkali; it has poor solubility in alcohol, ethyl acetate, acetone and ether; it is insoluble in benzene, petroleum ether, water, bicarbonate, sodium carbonate and ammonia. The caustic alkaline solution is colored yellow.

Found %: C 66.51, 66.55; H 4.97, 5.21; N 3.77, 3.83; OCH_3 16.12, 16.29. $C_{21}H_{19}O_6N$. Calculated %: C 66.14; H 4.98; N 3.67; OCH_3 16.29.

3-Nitro-4'-hydroxy-3',3"-dimethoxyfuchsone (II)

Into a four-necked flask, fitted with a stirrer and seal, a thermometer, a dropping funnel and a condenser topped by a calcium chloride tube, was introduced 25 g 3-nitro-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane and 150 ml dry ethyl acetate. The solution was cooled to a temperature of 0-2°, and addition was then made to it of 100 ml ethyl acetate containing 25 g dry hydrogen chloride. The solution turned red-violet. A solution of 20 ml freshly distilled amyl nitrite in 20 ml dry ethyl acetate was then stirred in gradually from the dropping funnel. With the addition of the first drop of solution the color changed to dark violet. The duration of the addition was 2 hours. Stirring at a temperature of 5-6° was continued for a further 3 hours and the reaction mass was left overnight at a temperature not higher than 15°. On the following morning the bottom of the flask contained an abundant, dark-violet precipitate of the hydrochloride. This was filtered off and washed with ethyl acetate and dry ether. For removal of the ethyl acetate it was left in dry ether for another few hours. The hydrochloride melted at 182-184° (with decomp.). Its chlorine analysis corresponds to 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone hydrochloride, containing one molecule of ether of crystallization.

Found %: Cl 7.29, 7.25. $C_{21}H_{17}O_6N \cdot HCl \cdot C_4H_{10}O$. Calculated %: Cl 7.26.

The hydrochloride is completely hydrolyzed by water in 2-3 hours. Its solution in 10% hydrochloric acid is almost completely hydrolyzed. When the hydrochloride is treated with sodium acetate solution it is also converted into the base after a few hours; after standing for a long period, the solution turns blue.

The base obtained by treating the hydrochloride with water is an orange, crystalline powder, with m.p. 227-228°. From glacial acetic acid it forms bright-orange crystals reminiscent of potassium bichromate in color; m.p. 228-229°. Its analysis corresponds to 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone.

Found %: C 66.36, 66.52; H 4.65, 4.67; N 3.71, 3.67. $C_{21}H_{17}O_6N$. Calculated %: C 66.49; H 4.48; N 3.69.

When the nitrofuchsone (II) is heated with 20% sodium bisulfite solution for 1-1½ hours at 60-70°, it partly goes into solution. The bisulfite compound does not crystallize from the solution. Addition of concentrated hydrochloric acid to the bisulfite solution brings down crystals of the hydrochloride of the nitrofuchsone contaminated by crystals of sodium chloride. Heating with hydrochloric acid gave a substance which did not yield the pure nitrofuchsone (II) after treatment with water; the substance has a low and prolonged melting range. The bisulfite solution becomes blue when treated with caustic alkali.

Hydrate form of 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone. 0.5 g 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone was dissolved in 20 ml glacial acetic acid and the solution was poured dropwise into 100 ml water. The resultant flocculent, orange precipitate was dried in a vacuum-desiccator over caustic alkali for 2 days. It melted with gradual shrinkage at 80-90°, after which it again solidified and finally melted at 227-228°. Its analysis for water of crystallization showed that it contains slightly less than 1 mole. It probably loses some water of crystallization in the desiccator.

Found %: H_2O 4.00, 4.08. $C_{21}H_{17}O_6N \cdot H_2O$. Calculated %: H_2O 4.53.

Recrystallization of the nitrofuchsone from glacial acetic acid gave a product melting at 228-229°. The hydrated form forms a bisulfite compound rather more quickly than the crystalline product, but a considerable proportion of the former likewise does not go into solution.

3-Nitro-4',4"-dihydroxy-3',3"-dimethoxytriphenylcarbinol (III)

1 g nitrohydroxydimethoxyfuchsone (II) was dissolved in 100 ml 5% sodium hydroxide to give a bright-blue solution. This was filtered. After 15-25 minutes it had lost the blue color and become red-orange and then brown. The color of the solution did not undergo any further change. The alkaline solution of the fuchsone was cooled while dropwise addition was made to it of 100 ml of 40% sodium bisulfite solution. A white flocculent precipitate was formed. This was filtered, washed with distilled water and dried on filter paper. A part of it was dried out in a vacuum-desiccator over sodium hyroxide. A slightly greyish powder was obtained with inclusions of orange material. Another portion was crystallized from aqueous acetone; when the solvent was slowly evaporated, white crystals came down in the form of cubes melting at 158-160°. The recrystallized material was kept in a desiccator for about a week and remained white, but afterwards turned yellow. The color of the uncrystallized precipitate changed to orange after only a day. Addition to the acetone solution of the carbinol of one drop of ammonia caused it to turn green, while one drop of concentrated hydrochloric acid turned it red-violet. The color hardly changed when dilute hydrochloric acid (2% solution) was added to the solution.

Found %: N 3.45, 3.54. $C_{21}H_{19}O_7N$. Calculated %: N 3.52.

3-Nitro-4',4"-diacetoxy-3',3"-dimethoxytriphenylcarbinol (IV)

To 2 g 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone was added 15 ml acetic anhydride and 0.5 g anhydrous sodium acetate; the solution was heated on a gauze to boiling for 3 hours, the color becoming light-orange and remaining so. After completion of the reaction, the solution was diluted with acetic acid and poured into ice water dropwise. The resultant slightly cream-colored, flocculent precipitate was not crystallized but was quickly washed with 2% sodium hydroxide solution, dissolved in acetic acid and the solution poured into water. It melted gradually between 76 and 80°.

Found %: $COCH_3$ 17.04; OH 3.85; N 2.91, 3.05. $C_{25}H_{23}O_9N$. Calculated %: $COCH_3$ 17.80; OH 3.53; N 2.91.

Analysis for the hydroxyl group by Tserevitinov's method confirmed the formation of the carbinol during acetylation.

Oxidative-alkaline cleavage of 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone

3-Nitro-4'-hydroxy-3'-methoxybenzophenone (V)

Into a 2-necked flask, fitted with a condenser connected at the top to a water jet pump and with a rubber stopper through which passed a bent tube reaching to the bottom of the flask, was introduced 2 g 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone (II) and 100 ml 5% sodium hydroxide solution. The bent tube was connected to two wash-bottles two-thirds filled with 20% sodium hydroxide solution. Aspiration of air was regulated by opening the pump so that not more than 2-3 bubbles passed through per second. The reaction flask was placed in a boiling water bath. After 15 hours a light-yellow precipitate had formed. The reaction flask was stood for a further 24 hours and then the precipitate was filtered off (0.8 g). It was dissolved in 30 ml water, the solution was filtered, and carefully neutralized (while cooling) with 40% acetic acid. 0.65 g of slightly pinkish precipitate was separated. It was crystallized from 5 ml alcohol to give slightly pinkish crystals with m.p. 132-134°. A second crystallization from alcohol raised the m.p. to 134-135°. Yield 0.4 g. A further recrystallization did not change the melting point.

The substance is soluble in the cold in caustic alkali to a bright-yellow solution; when heated it dissolves in 15% sodium carbonate solution with a green color; it does not dissolve on heating in 5% sodium carbonate solution, in bicarbonate and water, but the solvent takes on a greenish color. It dissolves in alcohol, acetone, ether and chloroform.

Its analysis corresponds to 3-nitro-4'-hydroxy-3'-methoxybenzophenone, not described in the literature. Its structure follows from the structure of the initial fuchsone and can only be 3-nitro-4'-hydroxy-3'-methoxybenzophenone.

Found %: C 61.77, 61.61; H 4.03, 4.17; N 5.18, 5.23. $C_{14}H_{11}O_5N$. Calculated %: C 61.54; H 4.03; N 5.12.

Indicator properties of 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone

We prepared buffer solutions from borax and monosubstituted potassium phosphate with pH from 6 to 7.6. The solutions were prepared in gradations of 0.1 pH. In addition, an 0.5% solution of 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone in acetone was prepared.

In a test tube were placed 10 ml buffer solution and 3-4 drops of the acetone solution of the dye. We observed sharp color changes at any pH interval:

at pH 6.4 the color was yellow, at pH 6.6, it was green, at pH 7.1 it was dark blue. The results were checked by titration.

3-Nitro-3',3",4',4"-tetramethoxytriphenylmethane (VI)

Into a thick-walled, round-bottomed flask were introduced 9 g 3-nitro-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane, 24 ml 10% sodium hydroxide and 7.2 ml dimethyl sulfate. The flask was vigorously shaken for 20-25 minutes. An oily substance separated out and later solidified to a clot. This was separated from the solution, pulverized, washed 2-3 times with 2% sodium hydroxide solution (5-10 ml each time) and then with water until the alkaline reaction had disappeared. The precipitate was dried and crystallized first from acetone and then from alcohol. There was obtained 7 g of yellow, finely crystalline product with m.p. 138-139° (73% of theory). The product gives a sharp depression of m.p. in the mixed melting test with the original nitro compound. It is insoluble in caustic alkali, very slightly soluble in alcohol and acetone.

Found %: N 3.68, 3.65; OCH_3 29.85, 29.80. $C_{23}H_{23}O_6N$. Calculated %: N 3.42; OCH_3 30.32.

3-Amino-3',3",4',4"-tetramethoxytriphenylmethane (VII)

5 g of (VI) was dissolved in 100 ml alcohol and to the solution was added 5 g skeletal nickel catalyst. The flask was connected to an apparatus filled with hydrogen and shaken on the machine. At the end of the reduction a considerable precipitate had formed. The reaction mixture was heated to the boil and the catalyst filtered off. Cooling of the filtrate led to separation of 2.3 g of substance. After driving off the solvent a further 1.7 g was obtained in the form of white needles with m.p. 126-127°. Yield 95% of theory. Repeated crystallization did not alter the melting point of the compound.

Found %: N 3.66, 3.77; OCH_3 32.42, 32.30. $C_{23}H_{25}O_4N$. Calculated %: N 3.69; OCH_3 32.74.

3-Amino-3',3",4', 4"-tetramethoxytriphenylmethane hydrochloride.

Treatment of the amine with 10% hydrochloric acid solution gave the water-insoluble hydrochloride. It crystallizes from alcohol with m.p. 230-232°; it is insoluble in concentrated and dilute hydrochloric acid, soluble in water when heated. The chlorine was determined by potentiometric titration.

Found %: Cl 8.50, 8.48. $C_{23}H_{25}O_4N \cdot HCl$. Calculated %: Cl 8.53.

SUMMARY

1. A series of hydroxytriphenylmethane compounds was synthesized.

2. The transformations of 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone were studied; its carbinol base and the product of its acetylation and oxidative cleavage were prepared.

3. The indicator properties of 3-nitro-4'-hydroxy-3',3"-dimethoxyfuchsone were studied. It shows a sharp color change in the pH region of 6.4 to 7.1 and may be recommended as an indicator for titration.

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* See Consultants Bureau translation, p. 897, 903, 1163.

** See Consultants Bureau translation, p. 161, 367, 569.

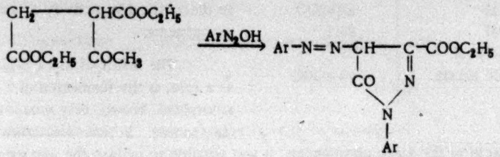
ACTION OF AROMATIC DIAZO COMPOUNDS ON COMPOUNDS OF THE TYPE OF ALKYLACETOACETIC ESTERS AS A METHOD OF SYNTHESIZING ARYL HYDRAZONES OF α-KETO ACIDS, α-AMINO ACIDS AND HETEROCYCLIC NITROGEN COMPOUNDS

XIII. REACTION OF DIETHYL α-ACETOGLUTARATE AND SOME OF ITS ANALOGS WITH ARYLDIAZONIUMS

V. V. Feofilaktov and N. K. Semenova

In a series of previous communications one of us demonstrated the possibility of applying the coupling reaction of aryldiazoniums with compounds of the type of alkylacetoacetic esters to the preparation of arylhydrazones of α-keto acids, as well as the application of the latter to the synthesis of α-amino acids [1-13] and indole derivatives [14].

It was also established that the arylhydrazones of esters of oxaloacetic acid, formed by coupling aryldiazoniums with acetosuccinic ester, spontaneously (even in process of their formation) were capable of ring closure to form a pyrazolone ring, and that the latter there and then again undergoes azo coupling with formation of azo compounds of the pyrazolone series [15,16]:

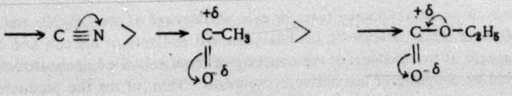


It appeared to be of interest to study the azo coupling of arylhydrazones with α-acetoglutaric ester and some of its analogs: γ,γ-diacetobutyric, α-carbethoxyglutaric and β-cyanoethylacetoacetic esters, and to make use of the resultant arylhydrazones for further syntheses. In particular we had in mind the investigation of the possibility of utilizing them for the synthesis of six-membered nitrogen heterocycles — pyridazinones — which have so far received little attention.

Coupling was performed in aqueous-alcoholic acetic acid, neutral or alkaline media, depending on the character and activity of the diazo and azo components. It was established that diazo components containing electrophilic substituents in the ring (p-nitroaniline, sulfanilic and anthranilic acids, etc.), also α- and β-naphthylamines, coupled in acetic acid and neutral media; diazo components containing nucleophilic substituents (toluidines) coupled in an alkaline medium, in agreement with statements in the literature [17].

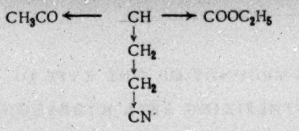
In our case the more active azo components proved to be β-cyanoethylacetoacetic and γ,γ-diacetobutyric esters, and the less active ones were α-acetoglutaric and α-carbethoxyglutaric esters. We arrive at this conclusion both on the basis of the ability of the former to couple in acetic acid and neutral media and on the basis of the higher yields of their coupling products, as can be illustrated by the reaction with phenyldiazonium chloride (Table 1).

The differing activity of these esters as azo components, as revealed in our experiments, can be correlated with the character and number of the groups activating the prototropic systems; as we know [18], these groups can be arranged in the following order in respect of their activating energy:



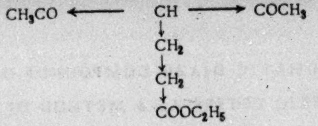
$$\longrightarrow C\equiv N \;>\; \longrightarrow \underset{\underset{O^{-\delta}}{\|}}{\overset{+\delta}{C}}-CH_3 \;>\; \longrightarrow \underset{\underset{O^{-\delta}}{\|}}{\overset{+\delta}{C}}-O-C_2H_5$$

On comparing the structures of the esters:



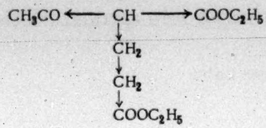
$CH_3CO \leftarrow CH(\downarrow CH_2 \downarrow CH_2 \downarrow CN) \rightarrow COOC_2H_5$

(A)



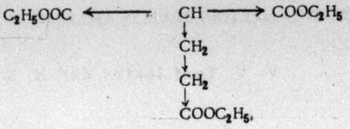
$CH_3CO \leftarrow CH(\downarrow CH_2 \downarrow CH_2 \downarrow COOC_2H_5) \rightarrow COCH_3$

(B)



$CH_3CO \leftarrow CH(\downarrow CH_2 \downarrow CH_2 \downarrow COOC_2H_5) \rightarrow COOC_2H_5$

(C)



$C_2H_5OOC \leftarrow CH(\downarrow CH_2 \downarrow CH_2 \downarrow COOC_2H_5) \rightarrow COOC_2H_5$,

(D)

we notice at once that among the activating groups of (A) and B) there are two each of the more active electrophilic groups (CN; CH_3CO), while the third contains only one of these (CH_3CO), and the fourth (D) contains three of these but the least active ones ($COOC_2H_5$). Hence the hydrogen of the CH groups in the first two compounds is more positive (labile) than in the third and fourth; this property is a factor in their differing activity as azo components.

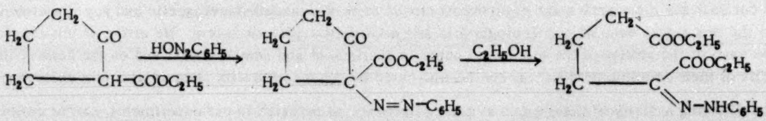
TABLE 1

Azo component	Coupling medium	Yield of hydrazone (%)
β-Cyanoethylacetoacetic ester	Neutral	98
γ,γ-Diacetobutyric ester	Neutral	90.1
α-Acetoglutaric ester	Acetic acid	71
α-Carbethoxyglutaric ester	Caustic alkali	49

The result of azo coupling, as a rule, is the formation of amorphous, brown, oily products (azo esters). In the case, however, of α-acetoglutaric ester and naphthionic acid as the diazo components, it was possible to isolate the azo esters in the solid form and to analyze them as the sodium salts (Table 2, Formula 12).

As a general rule, the process of coupling of all these esters was accompanied by separation of appreciable amounts (perceptible by the odor) of ethyl acetate. It is formed apparently by addition to some extent of alcohol (or alcoholate) to the acetyl group of the azo ester and subsequent cleavage of this group in the form of ethyl acetate. A similar type of alcoholysis at the $>C=O$ group was previously observed by one of us [14a] and by Hauser and Reynolds [19].

By carrying out the coupling of cyclopentanone carboxylic ester with diazobenzene in an alcoholic medium there is obtained, in addition to the phenylhydrazone of the acid ester of α-ketoadipic acid, a small amount of the phenylhydrazone of the diethyl ester of α-ketoadipic acid. Formation of the latter may be regarded as an unusual case of alcoholysis, although proceeding in presence of considerable amounts of water [14a]:



Hauser and Reynolds observed the addition of alcohol (in the form of alcoholate) to the benzoyl group of the ethyl ester of α-nitroso-α-benzoylvaleric acid and subsequent cleavage in the form of ethyl benzoate.

In the course of our research we also observed that the ease of cleavage of the CH_3CO- and C_2H_5COO-groups from the azo esters depends in large measure on the character and structure of the azo and diazo components. It is higher in the case of the products of the coupling of more active components and lower in the case of azo esters prepared by coupling of less active components. Thus, of the five products of coupling of phenyldiazonium chloride with various esters, only one (with β-cyanoethylacetoacetic ester) underwent

TABLE 2

Products of Coupling of α-Acetoglutaric Ester with Aryldiazoniums

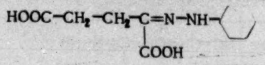
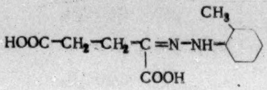
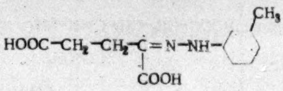
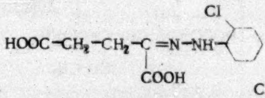
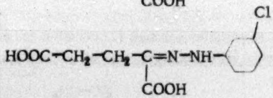
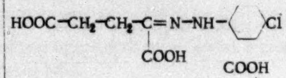
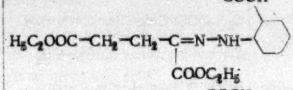
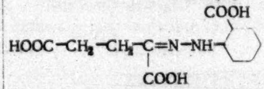
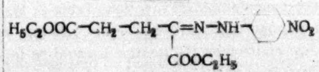
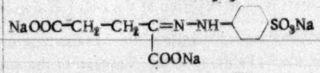
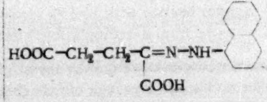
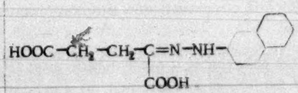
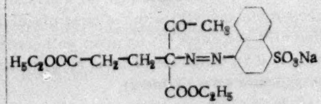
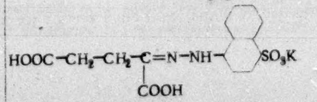
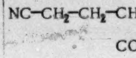
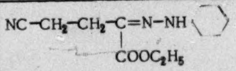
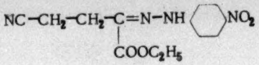
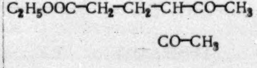
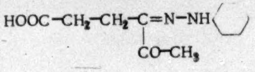
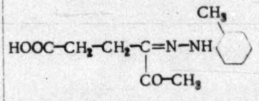
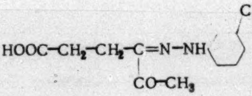
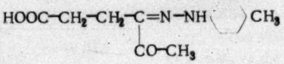
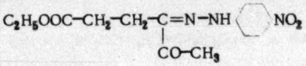
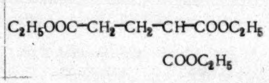
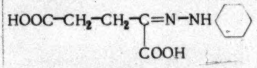
Prep. No.	Diazo component	Structure of product	M.p. (uncorrected)	Yield (%)
1	Aniline		152-153° [28]	74
2	o-Toluidine		159-160	88
3	m-Toluidine.		149	33.6
4	o-Chloroaniline. . .		183 [31]	60
5	m-Chloroaniline . .		170-171 [31]	72.1
6	p-Chloroaniline. . .		166	81
7	Anthranilic acid . .		104-105	57
7a	Ditto		225	–
8	p-Nitroaniline. . . .		137	87
9	Sulfanilic acid . . .		does not melt	95.3
10	α-Naphthylamine .		171	47.2
11	β-Naphthylamine. .		150	33.1
12	Naphthionic acid. .		does not melt	78.5
12a	Ditto.		does not melt	–

TABLE 3

Products of Coupling with Aryldiazoniums of Some Analogs of α-Acetoglutaric Ester

Prep. No.	Azo component	Diazo component	Structure	M.p.	Yield (%)
1	 $NC{-}CH_2{-}CH_2{-}CH(COCH_3){-}COOC_2H_5$	Aniline		159* [29]	98
2		p-Nitroaniline		158	98
3	 $C_2H_5OOC{-}CH_2{-}CH_2{-}CH(COCH_3){-}CO{-}CH_3$	Aniline		173-174	90.1
4		o-Toluidine		150	72.4
5		m-Toluidine		155	85.5
6		p-Toluidine		167	80.6
7		p-Nitroaniline		132	84.6
8	 $C_2H_5OOC{-}CH_2{-}CH_2{-}CH(COOC_2H_5){-}COOC_2H_5$	Aniline		152-153	49.1

spontaneous cleavage of the CH_3CO- group without supplementary reaction (Table 3; 1), whereas in the case of the products of coupling of γ,γ-diacetobutyric, α-acetoglutaric and α-carbethoxyglutaric esters, treatment was necessary with caustic alkali solution; for the first component the treatment could be less drastic (at room temperature or with gentle heating), but the others require reaction at the boil (on a water bath or gauze).

On the other hand, when the azo component was p-nitroaniline, then in the case of β-cyanoethylacetoacetic ester (Table 3; 2) and γ,γ-diacetobutyric ester (Table 3; 7) the cleavage of the acetyl group from the products of coupling proceeded spontaneously, and 10 minutes heating with 10-15% alcoholic solution of hydrochloric acid was only required for the azo esters prepared from α-acetoglutaric ester (Table 2; 8).

These observations of ours are in full accord with the conclusions from the investigations of M. M. Shemyakin and his coworkers [20-24] on the activating action on the hydrolytic cleavage of −C−C−bonds of electrophilic substituents and in particular of the NO_2 group, which in our experiments is readily transmitted through the conjugated double bond system of the benzene ring.

For the purpose of studying in more detail the behavior of α-acetoglutaric ester (I) during azo coupling and especially during subsequent saponification of the formed azo esters (II, V) a parallel study was made of the azo coupling of the ethyl ester of γ,γ-diacetobutyric acid (IV) with the same diazoniums. Saponification of the brown, amorphous products of azo coupling −the azo esters (V) * −gives well-crystallizable γ-arylhydrazones of β-pyruvylpropionic acid (VI; Table 3; 3,7), which are found to be quite different from the corresponding products of azo coupling of α-acetoglutaric ester (Table 2).

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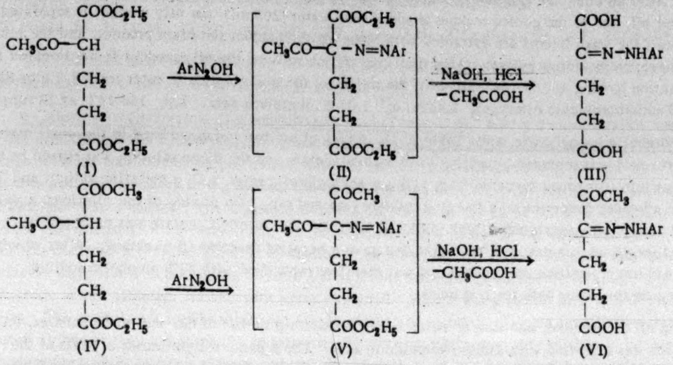
* This azo coupling reaction is likewise accompanied by formation of ethyl acetate (detected by odor).

Consequently, out of the two conceivable directions of hydrolytic cleavage of the azo esters (II) obtained from α-acetoglutaric ester, hydrolysis exclusively proceeds in the direction of cleavage of the acetyl groups (II ⟶ III), and does not proceed at all in the direction of cleavage of the carboethoxy groups (II ⟶ VI).



A comparative study of the behavior as azo components of α-carbethoxyglutaric ester and β-cyanoethylacetoacetic ester permitted the establishment of the advantages of some of these starting compounds for preparative purposes.

The prepared arylhydrazones were subjected to the following investigations:

a) Their transformation into indole derivatives, giving a comparatively convenient method for the synthesis of heteroauxin and its substituted products.

b) Reduction of some of them to glutamic acid, which on the whole, by extending to monoaminodicarboxylic acids the method of preparation of α-amino acids via the stage of the arylhydrazones of α-keto acids, gives a convenient method of synthesis of glutamic acid.

c) The ability of these arylhydrazones to cyclize to pyridazinone derivatives; investigations of some of the transformations of the latter.

EXPERIMENTAL

I. α-Acetoglutaric ester – Products of Its Azocoupling (Table 2).

α-Acetoglutaric ester was prepared by reaction of sodium ethyl acetoacetate with the ethyl ester of β-chloropropionic acid by the method of Clemo and Welch [25] as simplified by McIlwain and Richardson [26]. The ethyl ester of β-chloropropionic acid was synthesized by us from acrylonitrile by a slight modification of the known method [27].

Ethyl ester of β-chloropropionic acid. Into a round-bottomed 500 ml flask placed in a freezing mixture (ice and salt) is poured 53 g (1 mole) freshly distilled acrylonitrile. The flask is corked; through the cork passes a reflux condenser and through the latter is passed a glass tube reaching to the bottom of the flask. A dry stream of hydrogen chloride is run into the acrylonitrile through the tube until the weight increases by 43 g (instead of 36 g); this takes 12-13 hours. Into the flask is then introduced 55 ml concentrated hydrochloric acid (specific gravity 1.19), the mixture is shaken and allowed to stand. After 5-10 minutes, vigorous saponification commences with considerable heat development and separation of an abundant precipitate of ammonium chloride. After 30-40 minutes, the flask is heated for 20-25 minutes on the water bath, and then addition is made of 60 ml absolute ethyl alchol before continuing the heating for another 30 minutes. The cooled mixture is agitated with 125 ml cold water, the β-chloropropionic ester is separated, washed with 5% sodium carbonate solution and with water, dried with anhydrous sodium sulfate and distilled on an oil bath; a fraction is collected at 162-163°. Weight 105 g (78% calculated on the acrylonitrile).

Diethyl ester of α-acetoglutaric acid. Into a round-bottomed flask (500 ml), fitted with a reflux condenser and calcium chloride tube, is introduced 165 ml absolute ethyl alcohol and 11.5 g metallic sodium. To the cooled alcoholate is added 130 g ethyl acetoacetate, followed after stirring by 68 g ethyl ester of β-chloro propionic acid. After a few minutes a vigorous reaction commences to the accompaniment of strong heat development and separation of sodium chloride. After an hour, the mixture is heated on the water bath (until the alkaline reaction disappears), the alcohol is distilled off, and to the cooled residue is added cold water (200 ml); the oily product is separated and washed with cold water; the wash liquors are extracted with ether which dissolves the main product, and the ethereal solution is dried with anhydrous sodium sulfate. After distilling off the solvent, the oily product is fractionated in vacuum to give a fraction boiling at 163-164° (22 mm); the weight of the α-acetoglutaric ester was 98.5 g or 85% (calculated on the β-chloropropionic ester) n_D^{19} 1.4420; d_4^{19} 1.0695; literature data: b.p. 146-147° at 12 mm [26].

Phenylhydrazone of α-ketoglutaric acid (Table 2; 1). 4.65 g of aniline was diazotized in the usual manner; the excess hydrochloric acid was removed by adding solid sodium acetate and the diazo solution was stirred in a thin stream into the sodium compound prepared from 11.5 g α-acetoglutaric ester, 1.15 g metallic sodium and 30 ml alcohol, contained in a beaker immersed in a freezing mixture (ice and salt). On mixing of the solutions, a yellow emulsion was formed and quickly separated a thick, dark-red oil. The odor of ethyl acetate was perceptible. Stirring was continued for 40-50 minutes until the diazo test gave a negative reaction (β-naphthol), after which the oil was separated; it did not crystallize on standing and was therefore saponified with 20% alcoholic sodium hydroxide[*] by heating on the water bath for 1-1½ hours.

After distilling off the alcohol, addition of water and extraction with ether of the neutral impurities, the cooled alkaline solution was acidified with dilute hydrochloric acid. The separated light-brown crystals of the phenylhydrazone of α-ketoglutaric acid were separated, washed with water and dried. Weight 8.75 g (74% of the theoretical), m.p. 145-148°. After recrystallization from alcohol (with addition of carbon) and then from ethyl acetate, the light-yellow crystals of the phenylhydrazone melted at 152-153°,[**] in agreement with the literature [28].

Found %: N 11.71, 11.65. $C_{11}H_{12}O_4N_2$. Calculated %: N 11.86.

o-Tolylhydrazone of α-ketoglutaric acid (Table 2; 2). To a mixture of 5.3 g o-toluidine and 30 ml water in a beaker is added 13 ml concentrated hydrochloric acid followed by 40 g ice; the beaker is placed in a freezing mixture and at a temperature of −2 to −5° addition is gradually made of a solution of 3.6 g sodium nitrite in 14 ml water. After 10-15 minutes the diazotization is completed and the diazo solution is transferred with stirring into a beaker (immersed in freezing mixture and fitted with a mechanical stirrer) containing the sodium compound prepared from 11.5 g (0.05 mole) α-acetoglutaric ester, 4.6 g (0.2 g-atom) sodium metal and 60 ml absolute alcohol. A yellow emulsion forms and the smell of ethyl acetate is noticed. Stirring is continued for an hour (until the reaction for diazo compound is negative). The reaction product is a dark-red, oily azo ester; it is separated by decantation from the alcoholic liquor; the latter is acidified with HCl (to Congo) and twice extracted with ether; the ether is distilled off and the extract (about 0.4 g) is added to the azo ester. The combined product is dissolved in 40 ml 20 % alcoholic solution of sodium hydroxide and refluxed on a water bath. After a heating period of 2½ hours, 40 ml water is added to the flask and the alcohol is distilled off. After removal of the neutral impurities by ether extraction, the cooled alkaline solution is acidified with dilute hydrochloric acid. The precipitated dark-yellow crystals are collected, washed with water and dried. Weight 11.0 g. Yield 88%. M.p. 155-157° (with decomposition); after recrystallization from hot acetic acid or 50% aqueous alcohol with addition of carbon, the yellow star-like clusters of needles of o-tolyhydrazone of α-ketoglutaric acid melted at 159-160° with decompostion (uncorrected).

The compound is extremely soluble in acetone, readily soluble in ether, ethyl acetate, hot acetic acid and alcohol, poorly soluble in benzene; it forms a stable violet color with concentrated sulfuric acid and potassium bichromate (Bülow reaction).

Found %: N 11.01, 10.98, equiv. 122, 123. $C_{12}H_{14}O_4N_2$. Calculated %: N 11.20; equiv. 125.

m-Tolylhydrazone of α-ketoglutaric acid (Table 2; 3). 5.3 g m-toluidine was diazotized and coupled with the sodium derivative prepared from 11.5 g α-acetoglutaric ester by the previously described method. Saponification of the oily product of azo coupling was performed by heating with sodium alcoholate (4 g Na in 60 ml alcohol) for 2 hours. On the expiration of this period, addition was made to the flask of 100 ml water and the alcohol was distilled off. The neutral impurities were removed from the cooled alkaline solution by ether extraction and then the solution was carefully acidified (with ice cooling) with dilute hydrochloric acid. The resultant light-yellow crystals were collected, washed with water and dried. Weight 4.20 g (33.6 %), m.p. 146-148°. Readily soluble in methyl alcohol, ethyl alcohol, acetone and ethyl acetate. After recrystallization from aqueous ethyl alcohol, the m-tolylhydrazone of α-ketoglutaric acid melted at 149° with decomposition.

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[*] 40 % ethyl alcohol was normally used for the alcoholic alkali.

[**] The melting points given for our preparations were not corrected.

Found %: N 11.24, 11.30; equiv. 126, 127. $C_{12}H_{14}O_4N_2$. Calculated %: N 11.20; equiv. 125.

The obtained m-tolylhydrazone of α-ketoglutaric acid was converted into 1-(m-tolyl)-pyridazinone-3-carboxylic acid and 4-methyl-2-carboxyindole-3-acetic acid.

o-Chlorophenylhydrazone of α-ketoglutaric acid (Table 2; 4). 6.34 g o-chloroaniline was diazotized in the usual manner and the excess of hydrochloric acid removed with solid sodium acetate. With energetic stirring, the diazo solution was introduced portionwise into the cooled (with snow and salt) sodium derivative prepared from 11.5 g α-acetoglutaric ester, 1.15 g sodium and 30 ml absolute alcohol. The stirring was prolonged for an hour (until absence of free diazo). The separated dark-red oil was dissolved in 50 ml 25% alcoholic solution of potassium hydroxide and refluxed on the water bath. At the expiration of 4 hours, 30 ml water was added to the flask and the alcohol was distilled off. After removal of neutral impurities from the cooled alkaline solution by ether extraction, the solution was placed in a freezing mixture and acidified with dilute hydrochloric acid. The precipitated light-pink crystals were collected, washed with water and dried. Weight 8.1 g (60%), m.p. 176-179°, positive Bülow reaction. The crystals are highly soluble in ethyl acetate and acetone, dissolve readily in acetic acid and methyl and ethyl alcohols; they are insoluble in benzene, ligroin and ether; sparingly soluble in hot water. After recrystallization from alcohol (with carbon) and then from acetic acid, the bright-yellow needles melted at 183° with decomposition.

Found %: N 10.24, 10.22; equiv. 130,134. $C_{11}H_{11}O_4N_2Cl$. Calculated %: N 10.37; equiv. 135.

m-Chlorophenylhydrazone of α-ketoglutaric acid (Table 2; 5). 6.35 g m-chloroaniline was diazotized and coupled with the sodium derivative prepared from 11.5 g α-acetoglutaric ester in conditions similar to those employed with o-chloroaniline. After saponification of the dark-red oil, 9.75 g (72.1%) of dark-brown crystals was isolated, m.p. 166-168°. The crystals were readily soluble in ethyl and methyl alcohol, ether, acetone and ethyl acetate, much less soluble in benzene and ligroin, sparingly soluble in water. After three recrystallizations from 50% acetic acid in presence of carbon, the dark-red crystals of the m-chlorophenylhydrazone of α-ketoglutaric acid melted at 170-171° with decomposition and did not give Bülow's reaction.

Found %: N 10.32, 10.41; equiv. 132, 133. $C_{11}H_{11}O_4N_2Cl$. Calculated %: N 10.37; equiv. 135.

p-Chlorophenylhydrazone of α-ketoglutaric acid (Table 2; 6). 6.35 g p-chloroaniline was diazotized and coupled with the sodium derivative prepared from 11.5 g α-acetoglutaric ester in conditions similar to those employed for o-chloroaniline. The reaction product (a dark-red oil) was saponified with 50 ml 25% alcoholic potash by heating on the water bath for 5-6 hours. Acidification of the dilute alkaline solution gave 10.93 g (81%) yellow-pink crystals melting at 155-158° and not giving the Bülow reaction. The solubility was extremely good in acetone and ethyl acetate, good in ether, ethyl and methyl alcohols, hot acetic acid and boiling water; the product was insoluble in benzene. After two recrystallizations from boiling water in presence of carbon, the bright-yellow heavy crystals of the p-chlorophenylhydrazone of α-ketoglutaric acid melted at 166° with decomposition.

Found %: N 10.26, 10.55; equiv. 129, 133. $C_{11}H_{11}O_4N_2Cl$. Calculated %: N 10.37; equiv. 135.

o-Carboxyphenylhydrazone of diethyl α-ketoglutarate (Table 2; 7). 4.35 g anthranilic acid was mixed with 35 ml hot water to which was added 14 ml concentrated hydrochloric acid. The hydrochloride, cooled to −5°, was diazotized with 20% sodium nitrite solution (1.83 g in 8 ml water). Diazotization was continued for 20 minutes, after which the solution was kept in a freezing mixture for another 30 minutes (the excess of hydrochloric acid was not removed) and then transferred in a thin stream into a cooled solution of the sodium derivative of α-acetoglutaric ester with vigorous stirring. The sodium derivative was prepared from 5.8 g ester, 1.7 g sodium and 30 ml absolute alcohol. Mixing of the solutions caused a yellow emulsion to be formed, followed by separation of orange-colored oily drops and, finally, by a thick, dark-red oil; the odor of ethyl acetate was perceptible. After 40 minutes stirring, addition was made to the mixture of 10 % NaOH solution until the reaction was neutral, and stirring was continued for another 40 minutes. The dark-red oil was extracted with ether and kept at room temperature, after two days it had solidified but no crystals were observed. The solid red mass, apparently a sodium salt (combined at the nuclear COOH group), was heated with a small amount (5 ml) dilute acetic acid. This again converted it into a red oil. The latter was separated from the acetic acid and triturated with cold ethyl alcohol (10-15 ml). It then solidified to a light-yellow, finely granular mass which was drained, washed with water and dried. Weight

4.78 g (57%), m.p. 101-104°, positive Bülow reaction. The solubility of the crystals was good in alcohol, acetone, acetic acid and ligroin (from the latter they separated in the form of lustrous, pinkish needles), moderate in ether, and poor in benzene. After recrystallization from aqueous alcohol, the very slightly pink needles melted at 104-105° without decomposition.

Found %: N 8.09, 8.44; equiv. 333, 331. $C_{16}H_{20}O_6N_2$. Calculated %: N 8.33; equiv. 335.

o-Carboxyphenylhydrazone of α-ketoglutaric acid (Table 2, 7a). 3.35 g ester (m.p. 104-105°) after saponification with 10% aqueous alcoholic solution of sodium hydroxide gave 2.52 g (90%) yellowish-pink crystals of the o-carboxyphenylhydrazone of α-ketoglutaric acid, melting at 220-222°. The crystals gave a positive Bülow reaction. The product was insoluble in water and very sparingly soluble in organic solvents (alcohol, ether, ethyl acetate, benzene, acetone).

After several precipitations with water from solution in acetic acid, the substance melted at 225° with decomposition.

Found %: N 9.87, 9.91; equiv. 94.5, 94.9. $C_{12}H_{12}O_6N_2$. Calculated %: N 10.00; equiv. 93.4.

The composition and structure of the compound were confirmed by transformation into an indole derivative which proved to be identical with the indole derivative prepared from the o-carboxyphenylhydrazone of diethyl-α-ketoglutarate.

p-Nitrophenylhydrazone of diethyl α-ketoglutarate (Table 2; 8). 6.90 g p-nitroaniline was diazotized and after removal of the hydrochloric acid with sodium acetate it was coupled with the sodium derivative of α-acetoglutaric ester prepared from 11.5 g ester, 1.15 g sodium and 30 ml alcohol absolute, cooled with ice and salt. 10% sodium hydroxide was stirred into the solution until neutral to litmus. Stirring was continued for an hour (until the diazo reaction was negative). The odor of ethyl acetate was given off. The dark-red oil was separated, washed with water and allowed to stand; it did not crystallize and was therefore heated for 10-15 minutes with 20 ml 10% alcoholic solution of hydrochloric acid. On cooling, the oil then formed a dark-red crystalline mass. The crystals were triturated in a mortar with a small amount of ethyl acetate, drained, and washed on the filter with small portions of ethyl acetate. Weight of crystals 14.54 g (87%). M.p. 131-134°. The solubility of the crystals was good in hot acetic acid and hot alcohol, moderate in ethyl acetate, poor in ether and benzene. After two recrystallizations from acetic acid and then from absolute alcohol, the bright-yellow, slender needles of the p-nitrophenylhydrazone of diethyl α-ketoglutarate melted at 137° and did not give Bülow reaction.

Found %: N 12.31, 12.23. $C_{15}H_{19}O_6N_3$. Calculated %: N 12.46.

p-Sulfophenylhydrazone of α-ketoglutaric acid (trisodium salt; Table 2; 9). To 5.8 g sodium sulfanilate dissolved in 50 ml hot water was added 14 ml concentrated hydrochloric acid; portionwise addition was then made at −3° to the liquid, containing crystals of hydrochloride, of a solution of sodium nitrite (1.8 g nitrite in 8 ml water). At the expiration of 20 minutes, when the diazotization was complete, the crystals of diazosulfonate were quickly drained, washed with ice water, stirred into 50 ml cold water and introduced in small portions into the sodium derivative prepared from 5.75 g α-acetoglutaric ester, 0.57 g sodium and 15 ml absolute alcohol. After a period of 30 minutes from the start of the stirring-in, the coupling was completed; the beaker contents consisted of a transparent, dark-red solution. This was filtered and evaporated on a water bath. The residue of viscous, red oil was stirred with 30 ml ethyl alcohol and sodium hydroxide (2 g in 8 ml water). Orange crystals of salt came down after a few minutes and were drained and dried. Weight 7.0 g. Evaporation of the filtrate gave another 2.1 g light-orange crystals. Hence the total yield was 9.1 g (95.3 %). The solubility of the crystals is excellent in water, moderate in aqueous alcohol and nil in organic solvents (benzene, ligroin, ethyl acetate, acetone). The substance crystallized from aqueous alcohol in the form of yellow needlets with a tinge of pink, not containing water of crystallization and not giving the Bülow reaction. A test for sulfur gave a positive reaction.

Found %: N 7.02, 7.09. Na 17.65, 17.81. $C_{11}H_9O_7N_2SNa_3$. Calculated %: N 7.33; Na 18.06.

α-Naphthylhydrazone of α-acetoglutaric acid (Table 2; 10). A mixture of 2.86 g α-naphthylamine, 110 ml water and 12 ml concentrated hydrochloric acid in a porcelain beaker was gently heated (until all was dissolved) and then placed in a freezing mixture; at a temperature of 0 to +4° it was diazotized with sodium nitrite solution (1.4 g nitrite in 8 ml water). After 10 minutes from the completion of diazotization, addition was made to the diazo solution of the sodium compound prepared from 4.6 g α-acetoglutaric ester, 0.46 g sodium and 15 ml absolute alcohol. Dropwise addition was then made to the reaction mixture of a cooled 10% aqueous solution of sodium hydroxide until neutral to litmus. Coupling was completed in an hour. The red-violet oil was extracted with ether, the ether was distilled off and the residue of oil was saponified with 15% aqueous alcoholic solution of potassium hydroxide (25 ml). After heating for two hours, addition was made to the flask of water, and the alcohol was distilled off. The cooled solution was extracted with ether to remove neutral impurities and the solution was then diluted 20 times with water, cooled and acidified with 5% hydrochloric acid. The brownish flocs of the α-naphthylhydrazone of α-ketoglutaric acid were washed on the filter with water and dried in a vacuum-desiccator (since they darkened in the air). Weight 2.7 g (47.2%), m.p. 153-158°.

The compound showed good solubility in acetic acid, alcohol, ethyl acetate and acetone; moderate solubility in ether in the cold; poor solubility in benzene and ligroin. When the amorphous, brownish powder was heated with acetic acid, it changed into crystals. The latter, however, were difficult to purify. Repeated recrystallization from glacial acetic acid and then from 50% alcohol with addition of carbon gave light-orange thin plates melting at 170° with decomposition. A green color was produced with potassium bichromate and strong sulfuric acid.

Found %: N 9.59, 9.54; equiv. 139, 141. $C_{15}H_{14}O_4N_2$. Calculated %: N 9.79; equiv. 143.

β-Naphthylhydrazone of α-ketoglutaric acid (Table 2; 11). The diazo solution from 3.6 g β-naphthylamine, after elimination of excess hydrochloric acid with sodium acetate, was added to the sodium compound prepared from 5.75 g α-acetoglutaric ester. The viscous, bright-red oil resulting from coupling was saponified in conditions similar to those applied in the saponification of the azo ester from α-naphthylamine. Yield 2.4 g (33.1%) of the β-naphthylhydrazone of α-ketoglutaric acid in the form of a dark-colored, amorphous powder, decomposing at 140-144°. The product has good solubility in ethyl and methyl alcohols, ethyl acetate, acetic acid and acetone; moderate solubility in ligroin and hot benzene; poor solubility in ether. It is extremely difficult to purify, however. After repeated recrystallization from alcohol with addition of carbon, and then from acetic acid and ligroin, the β-naphthylhydrazone was in the form of a light-brown, amorphous powder, decomposing when heated to 150°.

Found %: N 9.53, 9.61; equiv. 138, 141. $C_{15}H_{14}O_4N_2$. Calculated %: N 9.79; equiv. 143.

Diethyl ester of α-(4-sulfonaphthyl-1-azo)-α-acetoglutaric acid (sodium salt; Table 2; 12). 5.6 g naphthionic acid was dissolved in aqueous sodium carbonate (2.8 g carbonate in 50 ml water). To the solution was added 12 ml concentrated hydrochloric acid (1.19) and, at −2°, a sodium nitrite solution (1.8 g nitrite in 8 ml water); a yellow paste of diazosulfonate was formed. This was drained, washed with ice water, mixed with 50 ml ice water and introduced, with rapid stirring, into a cooled (ice-salt) sodium compound prepared from 5.75 g α-acetoglutaric ester, 0.57 g sodium and 15 ml absolute alcohol.

Mixing of the solutions at first gave a reddish-orange emulsion which quickly disappeared; coupling was complete after 40 minutes. The reddish-brown, transparent liquid, containing the product of reaction, was filtered and evaporated on the water bath. Trituration of the residual reddish-brown oil with absolute alcohol caused the product to separate in the form of a dark-rose powder. Weight 9.3 g (78.5%). This product did not melt; it was moderately soluble on heating in ethyl alcohol (aqueous) and in methyl alcohol, readily soluble in water, insoluble in ethyl acetate, benzene, acetone and ligroin. It consisted of the sodium salt of the azo ester.

Found %: N 5.44, 5.68; Na 4.38, 4.32. $C_{21}H_{23}O_8N_2SNa$. Calculated %: N 5.76; Na 4.73.

4-Sulfonaphthyl-1-hydrazone of α-ketoglutaric acid (monopotassium salt; Table 2, 12a). 4.86 g of the above-described azo ester was heated for one hour on a water bath with 25 ml 20% alcoholic potash. After addition of water and removal of the alcohol, the cooled solution was acidified with dilute hydrochloric acid. Fine yellow, lustrous crystals came down after 5 minutes. Weight 3.7 g (91.4%). The substance has good solubility in acetic acid and poor solubility in acetone, benzene and ethyl acetate. After recrystallization from water (with carbon) and then from aqueous alcohol the 4-potassium sulfonaphthyl-1-hydrazone formed bright-yellow, infusible needles imparting a violet color to the nonluminous flame of a burner and leaving a mineral residue after burning. On carrying out the saponification with sodium hydroxide, the saponification product did not give a precipitate with hydrochloric acid. On the other hand, on adding to the alkaline solution, after saponification with sodium hydroxide, a solution of potassium hydroxide, a precipitate again failed to come down, but acidification of the latter solution with hydrochloric acid led to separation of the same lustrous, bronze-colored, scaly crystals of the monopotassium salt. The test for sulfur gave a positive reaction.

Found %: N 6.77, 6.63; K 9.41, 9.37; equiv. 197, 199. $C_{15}H_{13}O_7N_2SK$. Calculated %: N 6.91; K 9.65; equiv. 202.

II. β-Cyanoethylacetoacetic Ester — Some Products of Its Azo Coupling (Table 3)

The initial β-cyanoethylacetoacetic ester was synthesized in 77% yield by condensation of ethylacetoacetate with β-chloropropionitrile [29] and had the constants: b.p. (18 mm) 156°; (27 mm) 164-167°; d_{17}^{17} 1.0725; d_4^{17} 1.0705; $n_D^{17.5}$ 1.4474; MR_D 45.71; calculated for the keto form 45.37; for the enol form 46.42.

β-Cyanoethylacetoacetic ester was azocoupled with aniline and p-nitroaniline.

Phenylhydrazone of the ethyl ester of β-cyanomethylpyrotartaric acid (Table 3; 1). 9.3 g aniline was diazotized in the usual manner with sodium nitrite in presence of hydrochloric acid; the acid was removed by adding solid sodium acetate and the diazo solution was poured into β-cyanoethylacetoacetic ester (18.3 g) placed in a freezing mixture. With vigorous stirring, dropwise addition was then made from a dropping funnel of a cooled 10 % aqueous solution of sodium hydroxide until the reaction was neutral to litmus. The end of the reaction was signalized by the absence of free diazo compound (β-naphthol test) which usually required 40-60 minutes stirring. The dark-red oil was separated from the aqueous liquor, washed with water, stirred with 50 ml ethyl alcohol and left in an open beaker at room temperature. After 3 days it crystallized in dense, light-orange crystals; the crystallization process was accompanied by the separation (detected by odor) of acetic acid (cleavage of the CH_3CO group). The crystals of the phenylhydrazone of the ethyl ester of β-cyanomethylpyrotartaric acid were drained, washed with ether and dried. Weight 24.01 g (98%). After recrystallization from acetic acid, the pinky-yellow crystals melted at 159° and gave a positive Bulow reaction.

Found %: N 16.93, 16.99. $C_{13}H_{15}O_2N_3$. Calculated %: N 17.14. Keimatsu and Sugasawa, who were the first to prepare and describe this compound, report a m.p. of 155° [29]. With the aim, therefore, of obtaining fuller confirmation of the nature of the compound prepared by us as the phenylhydrazone of the ethyl ester of β-cyanomethylpyrotartaric acid, previously described by Keimatsu and Sugasawa, we saponified it and obtained the anticipated phenylhydrazone of α-ketoglutaric acid; we also subjected it to Fischer's indole ring-closure reaction and obtained the anticipated ethyl ester of 2-carbethoxyindolyl-3-acetic acid. Consequently conclusive evidence has been obtained that the compound melting at 159° is the phenylhydrazone of the ethyl ester of β-cyanomethylpyrotartaric acid.

2.45 g phenylhydrazone of the ethyl ester of β-cyanomethylpyrotartaric acid (m.p. 159°) was mixed with 20 ml aqueous 20% potassium hydroxide solution and refluxed on the water bath for 6 hours. The cooled alkaline solution was diluted with water and acidified with dilute hydrochloric acid. On standing in a freezing mixture, the dark-red crystals of the acid separated. Weight 1.4 g, m.p. 147-149°. After recrystallization from aqueous alcohol and then from ethyl acetate, the light-yellow crystals melted at 152-153° with decomposition. A mixture with our previous preparation of the phenylhydrazone of α-ketoglutaric acid (m.p. 152-153°) did not suffer a depression of melting point.

p-Nitrophenylhydrazone of the ethyl ester of β-cyanomethylpyrotartaric acid (Table 3; 2). 3.45 g p-nitroaniline was diazotized in the usual manner. The inorganic acid (HCl) was removed with sodium acetate, and the diazo solution was then introduced into the cooled sodium derivative of β-cyanoethylacetoacetic ester (4.6 g ester, 0.6 g Na and 20 ml absolute ethyl alcohol). Dropwise addition was made with stirring of a 10% aqueous solution of sodium hydroxide until neutral. The oil was extracted with ether, and after the lapse of two days when the solvent had evaporated, it crystallized in orange crystals; weight 7.1 g (98%), m.p. 154-156°; the solubility of the crystals is good in ethyl alcohol, acetic acid, ethyl acetate and acetone. After recrystallization from acetic acid and then from alcohol, the light-brown needles (in clusters) melted at 158°.

Found %: N 18.60, 18.58. $C_{13}H_{14}O_4N_4$. Calculated %: N 18.65.

III. Ethyl Ester of γ,γ-Diacetobutyric Acid and Some Products of Its Azo Coupling

This ester was synthesized from ethyl β-chloropropionate and acetylacetone by the procedure of Marsch [30] as simplified by us. To some cooled sodium ethylate (11.5 g Na and 160 ml absolute alcohol), contained in a round-bottomed flask fitted with a reflux condenser, was added 150 g freshly distilled acetylacetone, followed a few minutes later by 68 g ethyl β-chloropropionate. The mixture was heated on a water bath for 2½ hours until the reaction was over (absence of alkaline reaction). After distilling off the alcohol the flask contents were agitated with 200 ml cold water; the reaction product (a yellow oil) was separated, the aqueous solution was extracted with ether and the extract added to the oil. The ethereal solution was dried with anhydrous sodium sulfate. After distilling off the solvent, the oil was fractionated in vacuum. A fraction was collected which boiled at 153-154° (19 mm) or at 178° (43 mm) or at 182° (48 mm) [30]. Yield of twice-distilled ester 67 g (67 %). The literature reports a 50% yield [30].

The so-prepared ethyl ester of γ,γ-diacetobutyric acid had the constants: d_{16}^{16} 1.0668; d_4^{16} 1.0657; n_D^{17} 1.4528; MR_D 50.44; calculated for the keto form 50.16; for the enol form 51.16.

Azo coupling of this ester was performed with aniline, o-, m-, and p-toluidines and p-nitroaniline.

In the case of aniline and the three toluidines, the products of azo coupling — the γ-arylhydrazones of the ethyl ester of β-pyruvylpropionic acid (coupling takes place with cleavage of the acetyl group) — are amorphous and could only be characterized after saponification to the corresponding carboxylic acids (Table 3; 3 to 6); but in the case of p-nitroaniline the product of coupling — the γ-(p-nitrophenylhydrazone) of the ethyl ester of β-pyruvylpropionic acid — was crystalline with m.p. 132° (Table 3; 7).

In the conditions of Fischer's reaction, (heating with 50% sulfuric acid solution), these arylhydrazones apparently undergo closure of the indole ring in the normal manner: with separation of ammonium sulfate, there are formed water-insoluble, amorphous products whose purification and closer characterization, however, could not be undertaken by us.

γ-Phenylhydrazone of β-pyruvylpropionic acid (Table 3; 3). 4.7 g aniline was diazotized in the usual manner. The excess of hydrochloric acid was removed with solid sodium acetate; the diazo solution was gradually introduced into the sodium derivative of γ,γ-diacetobutyric acid ethyl ester (in a freezing mixture of snow and salt) prepared from 10 g ester, 1.15 g sodium and 20 ml absolute ethyl alcohol. When the solutions were mixed, a dark-red oil was formed and the odor of ethyl acetate was given off. The oil was saponified with 50 ml 10% alcoholic aqueous solution of sodium hydroxide by heating on the water bath for 30 minutes. After addition of water and distillation of the alcohol, the neutral impurities were extracted with ether and the cooled alkaline solution was acidified with dilute hydrochloric acid. The precipitated light-brown crystals were washed and kept in a desiccator. Weight 10.5 g (90.1%), m.p. 163-166° without decomposition. Very good solubility in ethyl and methyl alcohol, ethyl acetate and acetone; good solubility in acetic acid and ether; moderate solubility in hot ligroin and hot benzene. After 3 recrystallizations from ethyl alcohol, the light-yellow, slender needles melted at 173-174° and gave a pronounced Bülow reaction.

Found %: N 11.96, 11.84; equiv. 232, 231. $C_{12}H_{14}O_3N_2$. Calculated %: N 11.96; equiv. 234.

2.34 g phenylhydrazone with m.p. 173-174° was dissolved in 25 ml 50% alcoholic solution of sulfuric acid and refluxed for 20 hours (until the Bülow reaction was negative). The mixture darkened and toward the end of the reaction it had a dark-brown color. Under cooling, the precipitate of ammonium sulfate was drained off at the pump and the filtrate poured into ice water; the precipitated amorphous, dark-brown indole derivative (weight 1.82 g) had excellent solubility in alcohol, ether, ethyl acetate and acetone; it was insoluble in benzene or petroleum ether. Repeated efforts to bring it into a chemically pure form were in vain.

γ-(o-, m-, p-Tolylhydrazones) of β-pyruvylpropionic acid (Table 3; 4 to 6). 2.7 g o-, m-, p-toluidines were diazotized as in the previously described case of aniline (hydrochloric acid eliminated with sodium acetate) and coupled (in each individual case) with the sodium derivative prepared from 5 g γ,γ-diacetobutyric ester, 2.3 g sodium (0.1 g-atom instead of 0.025 g-atom) and 50 ml absolute alcohol. When the solutions made contact, the odor of ethyl acetate was detected and a dark-red, viscous oil was formed. The oil was saponified by heating with 10 % aqueous alcoholic sodium hydroxide; the precipitated Na salt of the hydrazone-acid was separated (poor solubility in cold water), washed with alcohol, dissolved in warm water and acidified with 5% hydrochloric acid. In all cases yellow crystals with the same outward appearance came down; they had good solubility in acetic acid, methyl and ethyl alcohols, ethyl acetate, acetone, and ligroin when heated.

The o-isomer gave 4.5 g crystals (72.4%) with m.p. 145-147°. After recrystallization from ligroin and then from alcohol, the bright-yellow needles melted at 150° and gave a marked Bülow reaction.

Found %: N 11.16, 11.12; equiv. 246, 248. $C_{13}H_{16}O_3N_2$. Calculated %: N 11.29; equiv. 250.

The yield of crude product from m-toluidine was 5.3 g (85.5%) with m.p. 149-153°. After recrystallization from acetic acid or alcohol, the product was in the form of small, light-yellow needles and melted at 155°. Bülow reaction negative.

Found %: N 11.09, 11.21; equiv. 248,247. $C_{13}H_{16}O_3N_2$. Calculated %: N 11.29; equiv. 250.

p-Toluidine gave 5 g of product (80.6%) with m.p. 162-165°. After recrystallization from alcohol, the p-tolylhydrazone formed slender, yellow needles melting at 167° and negative to the Bülow reaction.

Found %: N 11.14, 11.07; equiv. 247, 244. $C_{13}H_{16}O_3N_2$. Calculated %: N 11.29, equiv. 250.

Attempts to cyclize these arylhydrazones to the indole derivatives by heating with alcoholic sulfuric acid, as indicated above, ended in failure due to the difficulty of purifying the reaction products which were assumed to be indole derivatives.

γ-(p-Nitrophenylhydrazone) of the ethyl ester of β-pyruvylpropionic acid (Table 3; 7). 3.45 g p-nitroaniline was diazotized in the usual manner; the hydrochloric acid was removed with sodium acetate. The cooled diazo solution was brought into a solution of 5 g γ,γ-diacetobutyric ester in 20 ml alcohol. Into the mixture, cooled externally with snow and salt, with rapid operation of the stirrer was introduced dropwise a 10 % aqueous solution of sodium hydroxide until the reaction was neutral to litmus. Stirring was continued for an hour (until the diazo reaction was negative). The condensation product – a dark-red oil – was separated and washed with water; residual oil was extracted with ether and added to the main bulk; the ethereal solution was left to evaporate at room temperature. After two days the oil crystallized completely. The crystals were washed with ether and dried. Weight 6.0 g (84.6% of the theoretical), m.p. 126-130°. The solubility of the substance was good in acetic acid, ethyl acetate and ethyl and methyl alcohols, moderate in ligroin and benzene. After recrystallization from ethyl alcohol and then from ethyl acetate, the p-nitrophenylhydrazone of the ethyl ester of β-pyruvylpropionic acid formed orange needles melting at 132° without decomposition.

Found %: N 13.04, 12.96. $C_{14}H_{17}O_5N_3$. Calculated %: N 13.21.

The nitrophenylhydrazone (m.p. 132°) was heated with 50% alcoholic sulfuric acid and the ammonium sulfate precipitate was separated. The filtrate was poured into water and gave a brown, amorphous precipitate, readily soluble in the majority of organic solvents. It was impossible, however, to bring it into the chemically pure form.

Coupling of α-carbethoxyglutaric ester with phenyldiazonium (Table 3; 8). 2.32 g aniline was diazotized and brought into the cooled sodium derivative of α-carbethoxyglutaric ester (6.5 g ester, 0.58 g Na and 20 ml absolute alcohol). After stirring for ten minutes, dropwise addition was made of 10 % NaOH solution until the reaction was weakly alkaline. Stirring was continued for 40-50 minutes. The dark-red oily product of coupling was saponified with 25% alcoholic potassium hydroxide for 20-24 hours. Water was then added and the alcohol distilled off. After removal of the ether and the neutral impurities, the solution was carefully acidified with dilute hydrochloric acid; the precipitated crystals were washed and dried. Weight 2.90 g (49.1%), m.p. 145-149°. After recrystallization from ethyl alcohol (with carbon), the light-yellow crystals of the phenylhydrazone of α-ketoglutaric acid melted at 152-153°; it did not depress the m.p. of a preparation obtained by azo coupling of α-acetoglutaric ester.

Found %: N 11.75, 11.68. $C_{11}H_{12}O_4N_2$. Calculated %: N 11.86.

SUMMARY

1. A study was made of the coupling of α-acetoglutaric, γ,γ-diacetobutyric, α-carbethoxyglutaric and β-cyanoethylacetoacetic esters with various aryldiazoniums; it was established that the reaction products are dark-red oily substances which in the majority of cases do not crystallize; they are azo esters which change into the aryldiazoniums when treated with caustic alkali.

2. The greatest activity in the coupling reactions is manifested by β-cyanoethylacetoacetic ester and α-acetoglutaric ester; considerations about the probable cause of this behavior are advanced.

3. Hydrolysis of the $>C-C<$ bond proceeds with maximum ease in the case of azo esters formed by the more active azo and diazo components.

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CONDENSATION OF ar-1-METHOXYTETRAHYDRONAPHTHALENE WITH FATTY ACID CHLORIDES

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For the preparation of (ar-1-hydroxytetrahydronaphthyl-4)-alkyl ketones ($HOC_{10}H_{10}COR$; R = alkyl) one of us [1] previously made use of the Fries rearrangement of ar-1-acyltetralols; it was then found that the reaction yields a mixture of ar-1,2- and ar-1,4-hydroxy ketones in which the ar-1,2-isomer greatly predominates; with increasing size of the acyl residue, the yield of (ar-1-hydroxytetrahydronaphthyl-4)-alkyl ketones sharply decreases.

On the basis of literature data [2] it could be assumed that in the condensation of ar-1-alkoxytetrahydronaphthalenes with acid chlorides in presence of aluminum chloride, the acyl group would be directed preferentially to the 4-position of the ring, and this route would offer the possibility of preparing (ar-1-alkoxytetrahydronaphthyl-4)-alkyl ketones and from them the corresponding hydroxy ketones in satisfactory yield. In this investigation we carried out a series of experiments on the condensation of ar-1-methoxytetrahydronaphthalene with chlorides of various fatty acids (acetic, propionic, butyric and palmitic); in this work, in accordance with expectation, (ar-1-methoxytetrahydronaphthyl-4)-alkyl ketones were obtained in yields of 60-80% of the theoretical.

The reaction was conducted in nitrobenzene solution with cooling. Formation of the isomeric (ar-1-methoxytetrahydronaphthyl-2)-alkyl ketones was not observed. The reaction was accompanied by slight resinification of the materials with consequent reduction to some extent of the yield of ketones.

Difficulties were encountered in splitting off the methoxyl group from the prepared ketones. The application for this purpose of the usual methods of dealkylation (heating with hydrogen halides) led to resinification. Moreover the hydrolysis of the methoxyl group appeared to be accompanied by cleavage of the acyl group, for in some cases ar-1-tetralol was isolated from the resinous products.

The required objective was reached by heating the methoxy ketones with $AlCl_3$ in benzene solution, when (ar-1-hydroxytetrahydronaphthyl-4)-alkyl ketones were obtained in a yield of 55-80% of the theoretical. But even in these conditions, cleavage of the acyl group was sometimes observed.

The structure of the (ar-1-hydroxytetrahydronaphthyl-4-)-alkyl ketones prepared by this route, and consequently also of the initial methoxytetrahydronaphthyl-(alkyl ketones), was established by comparison of the hydroxy ketones with the (ar-1-hydroxytetrahydronaphthyl-4-)-alkyl ketones synthesized by the Fries reaction.

The physicochemical and chemical properties of the (hydroxytetrahydronaphthyl)-alkyl ketones prepared by the different methods proved to be identical and no depression was observed in the melting point of mixed specimens.

EXPERIMENTAL

Ar-1-methoxytetrahydronaphthalene was prepared by two methods: 1) By the action of dimethyl sulfate on ar-1-tetrahydronaphthol in an aqueous alkaline medium [2]; 2) by catalytic hydrogenation of 1-methoxynaphthalene in alcoholic solution in presence of Raney nickel at a pressure of 90-100 atm. and a temperature of 130° [3].

(Ar-1-methoxytetrahydronaphthyl-4)-methylketone

30 g ar-1-methoxytetrahydronaphthalene was dissolved in 240 ml nitrobenzene and addition made with cooling and stirring of 14.5 g acetyl chloride (2.5% excess). Into the obtained solution at 0° was stirred, over a period of one hour, 30 g $AlCl_3$ (50% excess). Stirring was continued for another 4 hours and the mass left for 24 hours at room temperature, after which the reaction mass was poured into a mixture of ice and hydrochloric acid. The nitrobenzene and ethereal solutions were combined, the ether was first distilled off, and then the nitrobenzene (with steam). The residue after distillation of the nitrobenzene was extracted several times with ether. The ether extract was washed with 5% sodium hydroxide, then with water, and dried with sodium sulfate. The ether was driven off and the residue distilled in vacuum; b.p. 147-148° at 3 mm; yield 26.1 g (82.6% of theory).

After a second distillation the b.p. was 152-153° at 5 mm. Yield 24.5 g (77.5% of theory).

3.479 mg substance: 9.755 mg CO_2; 2.498 mg H_2O. 4.444 mg substance: 12.364 mg CO_2; 3.121 mg H_2O. Found %: C 76.47, 75.87; H 8.03, 7.86. $C_{13}H_{16}O_2$. Calculated %: C 76.43; H 7.90.

(Ar-1-hydroxytetrahydronaphthyl-4)-methylketone

5 g (ar-1-methoxytetrahydronaphthyl-4)-methyl ketone was dissolved in 200 ml absolute benzene. To the benzene solution was added 10 g $AlCl_3$. The reaction liquid was heated on the water bath at the boil for 6 hours and then poured into dilute hydrochloric acid and ice. The benzene layer was separated. The aqueous layer was extracted with ether and the ether extract combined with the benzene solution. The ether-benzene solution was washed several times with 8% potassium hydroxide solution. The alkaline solution was acidified with hydrochloric acid (1:1). The precipitated hydroxy ketone was filtered off and washed with water; m.p. 154-155°. Yield 3.8 g (82.6% of theory).

A melting point test on the mixture of the prepared compound with a specimen of (ar-1-hydroxytetrahydronaphthyl-4)-methyl ketone prepared by the Fries method did not give a depression.

(Ar-1-methoxytetrahydronaphthyl-4)-ethylketone

80 g ar-1-methoxytetrahydronaphthalene was dissolved in 640 ml dry nitrobenzene and addition was made, with cooling and stirring, of 60 g propionyl chloride (30% excess). The obtained solution was cooled and addition was made, at 0° and with stirring for one hour, of 75 g $AlCl_3$ (50% excess). Stirring was then continued for 4 hours, after which the mass was left at room temperature for 24 hours before being decomposed in the usual manner. The nitrobenzene layer was separated and the aqueous layer extracted with ether. The combined ethereal and nitrobenzene solutions were washed with 5% sodium hydroxide solution and then with water. The ether and nitrobenzene were distilled off the latter with steam. The residue was extracted with ether. The ethereal solution was dried with sodium sulfate, the ether distilled off, and the residue distilled in vacuum. B.p. 169-180° at 10 mm. Yield 28 g (7% of theory).

A second distillation gave b.p. 169-171° at 10 mm. Yield 26 g. The product crystallized on standing: m.p. 36-37°.

3.708 mg substance: 10.432 mg CO_2; 2.785 mg H_2O. Found %: C 76.72; H 8.40. $C_{14}H_{18}O_2$. Calculated %: C 77.02; H 8.31.

(Ar-1-hydroxytetrahydronaphthyl-4)-ethylketone

5.5 g (ar-1-methoxytetrahydronaphthyl-4)-ethylketone was dissolved in 100 ml benzene and 11 g $AlCl_3$ added; the reaction mass was heated for 5 hours at the boil. After cooling, the reaction mass was poured into a mixture of hydrochloric acid (1:1) and ice. The benzene layer was separated, and the aqueous layer extracted with ether. The ethereal and benzene solutions were combined, washed with water and shaken several times with 8% potassium hydroxide solution; the solution was then washed with water again. The aqueous solution was combined with the alkaline one and the aqueous-alkaline solution was acidified. The precipitate was filtered and dried. Yield 2.7 g (55% of theory); m.p. 152-153°.

No depression was observed in a melting point determination on a mixture of this compound with the (ar-1-hydroxytetrahydronaphthyl-4)-ethylketone prepared by the Fries rearrangement.

The ether-benzene solution was dried, the solvents were driven off and the residue distilled in vacuum. Yield 1.2 g with b.p. 118-120° at 15 mm. This b.p. is close to that of ar-1-methoxytetrahydronaphthalene.

Experiment on cleavage of the methoxyl group with aid of hydrogen bromide

2 g (ar-1-methoxytetrahydronaphthyl)-ethylketone, 60 ml glacial acetic acid, and 16 ml hydrogen bromide (48%) were heated at the boil for 3 hours, after which the reaction mass was poured on to ice and worked up with ether. The ether extract was washed several times with potassium hydroxide solution, the alkaline solution acidified, and the resultant precipitate filtered off. Yield 0.5 g with m.p. 63-65°.

No depression was observed in the mixed melting test with ar-tetrahydronaphthol.

Ar-(1-methoxytetrahydronaphthyl-4)-propylketone

Into a three-necked flask, fitted with a mechanical stirrer and a side tube, was introduced 21.6 g ar-1-methoxytetrahydronaphthalene dissolved in 180 ml dry nitrobenzene. To the solution, cooled with ice and stirred, was added 14 g butyryl chloride, followed by 22 g $AlCl_3$ in small portions over a period of $1\frac{1}{2}$ hours. After all the $AlCl_3$ had been added, the stirring was continued for another 4 hours, and decomposition effected as usual. Further working-up was similar to that in the preceding experiments on the condensation of ar-1-methoxytetrahydronaphthalene with acid chlorides.

A substance with b.p. 184-186° at 13 mm was obtained; yield 20.8 g (67.9% of the theoretical). On cooling, the compound solidified to a buttery mass.

3.323 mg substance: 9.452 mg CO_2; 2.589 mg H_2O. Found %: C 77.57; H 8.71. $C_{15}H_{20}O_2$. Calculated %: C 77.55; H 8.68.

Ar-(1-hydroxytetrahydronaphthyl-4)-propyl ketone

11 g ar-1-methoxytetrahydronaphthyl-4 propylketone was dissolved in 20 ml benzene. The solution was added to a mixture of 22 g $AlCl_3$ and 180 ml benzene. The reaction mass was heated for 6 hours at the boiling point of benzene and then poured, with cooling, into a mixture of hydrochloric acid (1:1) and ice. The benzene layer was separated and the aqueous layer extracted with ether. The benzene and ether extracts were combined and the benzene and ether were distilled off. The residue was dissolved in a little ether and the ethereal solution washed several times with 5-7% potassium hydroxide solution. At first the alkaline layer was deeply colored. The ethereal solution was washed with water, the aqueous solution was added to the alkaline solution, and the whole acidified with hydrochloric acid (1:1). The precipitate was filtered. Yield 6.2 g (60.7% of the theoretical); m.p. 131-132°.

No depression was observed in the mixed melting test with a specimen of the hydroxytetrahydronaphthyl-propylketone prepared by the Fries rearrangement.

Ar-1-palmitoyl-1-methoxytetrahydronaphthalene

Palmityl chloride was prepared from palmitic acid and thionyl chloride; b.p. 178-179°.

Into a three-necked flask, fitted with a mechanical stirrer and side tube, were introduced 25.8 g ar-1-methoxytetrahydronaphthalene and 200 ml nitrobenzene. To the solution was added, with cooling, 15.2 g palmityl chloride, followed gradually by 26 g $AlCl_3$ in the course of an hour; the reaction mass was then stirred for another 4 hours and left to stand for 18-20 hours. The viscous, dark-red solution was decomposed in the usual manner. Ether was added to facilitate separation of the layers. The ether-nitrobenzene layer was separated from the aqueous layer and washed with 8% KOH solution. The ether-nitrobenzene layer was transferred to a flask and the ether distilled off on a water bath, after which the nitrobenzene was distilled in steam. The residual oil was extracted with ether. The ether extract was washed with water and dried, and the residue distilled in vacuum. Two fractions were collected: 1) b.p. up to 220° at 0.15 mm; 2) b.p. 220-240° at 0.15 mm.

A second distillation yielded the following fractions: 1) b.p. 200-214° at 0.08 mm (12 g); 2) b.p. 214-216° at 0.08 mm (16 g).

The substance with b.p. 214-216° at 0.08 mm is the supposed ar-4-palmitoyl-1-methoxytetrahydronaphthalene, a light-yellow oil which solidified on cooling.

3.301 mg substance: 9.790 mg CO_2; 3.337 mg H_2O. Found %: C 80.88; H 11.31. $C_{27}H_{44}O_2$. Calculated %: C 80.95; H 11.07.

SUMMARY

1. Condensation of ar-1-methoxytetrahydronaphthalene with fatty acid chlorides in presence of $AlCl_3$ gives (ar-1-methoxytetrahydronaphthyl-4)-alkyl ketones in yields of 60-80% of the theoretical.

2. Dealkylation of (ar-1-methoxytetrahydronaphthyl-4)-alkyl ketones gave compounds identical with the (ar-1-hydroxytetrahydronaphthyl-4)-alkyl ketones prepared by the Fries method. Yields were 55-80% of the theoretical.

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DERIVATIVES OF 2,4-DIAMINO-1,3,5-TRIAZYLALKYLCARBOXYLIC ACIDS. I.

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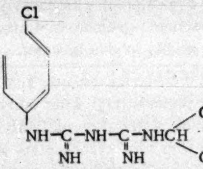
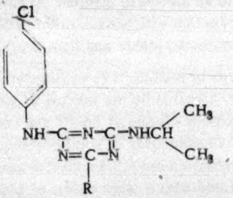
As far back as 1874, Nencki [1] established that the heating of guanidine salts of fatty acids leads to new compounds which he called guanamines. For example, on heating the guanidine salt of formic acid, formoguanamine is formed; the salt of acetic acid gives acetoguanamine, and so on. These compounds were accurately identified by Weith [2] and Claus [3] as derivatives of 2,4-diamino-1,3,5-triazine. Later Bamberger and Dieckmann [4] made a detailed study of this reaction and showed that the formation of guanamines proceeds through an intermediate biguanide. It was consequently established that derivatives of 2,4-diamino-1,3,5-triazines can be more conveniently prepared by starting from biguanides. In 1910 Rackmann [5] showed that biguanides have an extraordinarily high guanamine-forming tendency, formoguanamine being formed quantitatively by simple heating of free biguanide with an alcoholic solution of ethyl formate. The reaction proceeds similarly with benzoyl chloride. With dicarboxylic acids, however, the triazine ring does not close and the corresponding oxalyl-, malonyl-, succinyl-, etc. biguanides are formed.

A series of papers on the exploitation of the formation of 2,4-diamino-1,3,5-triazines was published by Ostrogovich and co-workers [6] who extended the reaction to nitriles, amides and amidines. It is interesting to note that Ostrogovich succeeded in extending this triazine ring closure reaction to acyl derivatives of biuret to form 2-aryl- or aralkyl-4,6-dihydroxy-1,3,5-triazines. Thus the tendency of the N—C—N—C—N grouping to form a six-membered ring is very great and even extends to oxygen-containing compounds.

A series of patents have been published in recent years [7,8] which use this ability to biguanides to condense with various derivatives of esters containing groups such as $-CN$, $-COOR$, $-SO_3H$, $-NO_2$.

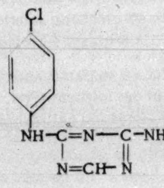
We were interested in derivatives of 2,4-diamino-1,3,5-triazine because of their structural similarity to bigumal (paludrine) or N'-p-chlorophenyl-N^5-isopropylbiguanide:



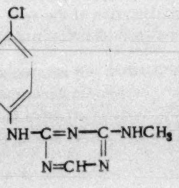


which is distinguished by high antimalarial activity. We undertook the synthesis of a group of triazine derivatives from biguanides by closure of the triazine ring with the objective of examining the effect of this closure on antimalarial activity.

Starting from the corresponding biguanides, V. N. Sokolova has prepared 2-amino-4-p-chlorophenylamino-1,3,5-triazine (I), 2-methylamino-4-p-chlorophenylamino-1,3,5-triazine (II), and 2-isopropylamino-4-p-chlorophenylamino-1,3,5-triazine (III):



(I)



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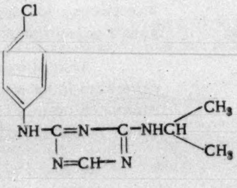
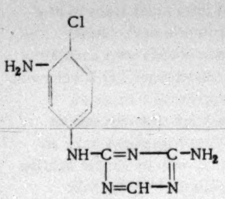
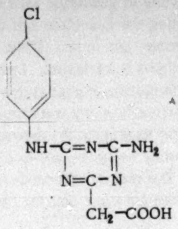
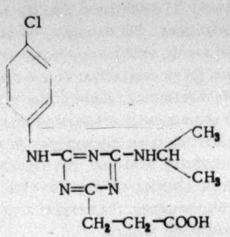


(III)

Since these compounds possessed weak antimalarial activity and were characterized by very poor solubility in water, while their salts were most unstable and suffered complete hydrolysis, we set ourselves the task of eliminating the solubility factor as a possible cause of the low activity by preparing compounds of the same type but exhibiting better solubility in water. Improved water solubility should be attainable by: 1) introduction of the amino group into the benzene ring and the preparation, from the resultant base, of stable salts; 2) introduction of alkylcarboxylic acid groups into the triazine ring and transformation of the acids into their salts. In the pursuit of our objective the compounds (IV), (V) and (VI) were synthesized:

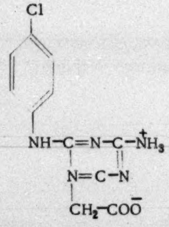

(IV)


(V)


(VI)

2-Amino-4-(p-chloro-m-aminophenyl)-amino-1,3,5-triazine (IV) was prepared from 4-chloro-3-nitroaniline; the latter was obtained by the method of Claus and Stiebel [9], slightly modified by us. Reaction of 3-nitro-4-chloroaniline hydrochloride with dicyanodiamide in an aqueous medium in Cohn's conditions [10] gave p-chloro-m-nitrophenyl-biguanide in good yield. We effected the first of the two above-mentioned syntheses by reducing the nitro group to the amino group and cyclizing the p-chloro-m-aminobiguanide to the triazine with the help of ethyl formate. Experiments on catalytic reduction with skeletal nickel catalyst, however were unsuccessful. Although hydrogen absorption proceeded normally, the reduced compound resinified at extraordinary speed even in a nitrogen atmosphere and it was impossible to isolate a pure substance from the resin. We therefore decided to close the triazine ring in the first place and then to reduce the nitro group. Reaction of p-chloro-m-nitrophenyl-biguanide with ethyl formate in an alcoholic medium [5] gave 2-amino-4-(p-chloro-m-nitrophenyl)-amino-1,3,5-triazine, which by catalytic reduction with palladium-on-carbon gave 2-amino-4-(p-chloro-m-aminophenyl)-amino-1,3,5-triazine. This base was perfectly stable and its hydrochloride was readily soluble in water.

We realized the synthesis of 2-amino-4-(p-chlorophenyl)-amino-1,3,5-triazine-6-acetic acid (V) by starting from p-chlorophenyl-biguanide, prepared by the method of Strukov and coworkers [11]. After recrystallization from water, p-chlorophenylbiguanide melted at 96-97° and contained 1 mole water of crystallization. Its anhydrous form melted at 128-129° [12]. Condensation of p-chlorophenylbiguanide with ethyl cyanoacetate gave a good yield of 2-amino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-acetonitrile. Saponification of the nitrile proceeds with some difficulty. When heated with a large excess of 16% NaOH solution, the nitrile went into solution after 3 hours and the free acid was then separated in 90% yield. 2-Amino-4-(p-chlorophenyl)-1,3,5-triazyl-6-acetic acid is an inner salt and therefore has a very high melting point (326-327°); it may be represented by formula (Va).


(Va)

The synthesis of 2-isopropylamino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-propionic acid (VI) was effected by condensation of N'-p-chlorophenyl-N^5-isopropyl-biguanide with the half ester acid chloride of succinic acid. Closure of the triazine ring proceeded through the acid chloride group and the reaction gave the ethyl ester of 2-isopropylamino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-propionic acid. Saponification of the ester with 4% alcoholic solution of NaOH gave 2-isopropylamino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-propionic acid.

Tests of the described new compounds for antimalarial activity were carried out in the chemotherapeutic department of our institute (Prof. G. N. Pershin) on strains of Plasmodium relictum and Plasmodium gallinaceum and did not reveal any active compounds among them.

EXPERIMENTAL

1. 4-Chloro-3-nitroaniline [9]. 100 g 4-chloroaniline was dissolved in 500 ml concentrated sulfuric acid and was nitrated (while cooling with ice and salt) with a mixture of 35 ml nitric acid (specific gravity 1.51) and 350 ml concentrated sulfuric acid. Nitration was conducted as quickly as possible at a temperature not exceeding 0°. The reaction mass was poured on to ice and neutralized with sodium carbonate. The precipitated 4-chloro-3-nitroaniline was purified by fractional crystallization from 10% methyl alcohol. Yield 79 g (58.5% of theory). M.p. 104-105°.

2. N-(4-Chloro-3-nitrophenyl)-biguanide. a) A mixture of 10 g 4-chloro-3-nitroaniline, 5 g dicyanodiamide and 7 ml 30% hydrochloric acid was heated at the boil for $5\frac{1}{2}$ hours on a glycerol bath [11]. The biguanide hydrochloride, which came down when the solution was cooled, was filtered off, washed with a little water and recrystallized from 30 ml water. Weight 12.8 g, m.p. 223-224.5°. The free base was isolated by adding a concentrated NaOH solution to the aqueous solution of the hydrochloride at 80-90°. Yield 11 g (74.7% of the theoretical). The m.p. depends on the speed of heating; at the rate of 2° per minute, the m.p. is 169-170°.

Biguanide base crystallizes with 1 molecule of water in the form of long prisms with an orange color. It loses water after prolonged drying at 100° and the color changes to yellow. It has good solubility in cold acetone, methyl and ethyl alcohols, ethyl acetate and glacial acetic acid; it is nearly insoluble in benzene, chloroform and petroleum ether.

0.1052 g substance: 4.12 ml 0.1 N HCl. Calculated: 4.08 ml 0.1 N HCl. 5.009 mg substance: 11.66 ml 0.01 g H_2SO_4. 5.167 mg substance: 12.14 ml 0.01 N H_2SO_4. Found %: N 32.59, 32.89. $C_8H_9O_2N_6Cl$. Calculated %: N 32.74.

3. 2-Amino-4-(*p*-chloro-*m*-nitrophenyl)-amino-1,3,5-triazine. 12.1 g N-(4-chloro-3-nitrophenyl)-biguanide was dissolved in 50 ml absolute alcohol and to the solution was added 4.5 ml ethyl formate. The solution was heated at the boil for $4\frac{1}{2}$ hours. The precipitate was filtered, washed with alcohol, and recrystallized from 75% acetic acid. Yield 7 g (56% of the theoretical). Yellow powder, m.p. 274-275.5°, almost insoluble in water and organic solvents, soluble in glacial acetic acid.

4.822 mg substance: 10.72 ml 0.01 N H_2SO_4. 4.929 mg substance: 10.89 ml 0.01 N H_2SO_4. Found %: N 31.12, 30.93. $C_9H_7O_2N_6Cl$. Calculated %: N 31.52.

4. 2-Amino-4-(*p*-chloro-*m*-aminophenyl)-amino-1,3,5-triazine. 5.2 g 2-amino-4-(*p*-chloro-*m*-nitrophenyl)-amino-1,3,5-triazine in 110 ml 3.5% hydrochloric acid was reduced with hydrogen at room temperature in presence of palladium catalyst (0.05 g palladium chloride on 2 g active carbon) with mechanical shaking for 6 hours. 1,300 ml hydrogen was absorbed. The substance went into solution. The solution was filtered and evaporated to dryness in vacuum. The triazine hydrochloride (weight 5.3 g) was recrystallized from 20 ml water. The cream-colored powder, m.p. 255-257°, had good solubility in water.

0.1536 g substance: 9.4 ml 0.1 N NaOH. Calculated: 9.9 ml 0.1 N NaOH. 4.942 mg substance: 9.36 ml 0.01 N H_2SO_4. 5.178 mg substance: 9.81 ml 0.01 N H_2SO_4. 8.360 mg substance: 7.546 mg AgCl. 7.823 mg substance: 7.128 mg AgCl. Found %: N 26.52, 26.39; Cl 22.33, 22.53. $C_9H_9N_6Cl \cdot 2HCl$. Calculated %: N 27.14; Cl 22.94.

The free base was isolated by treatment of the aqueous solution of the hydrochloride with NaOH solution until weakly alkaline to litmus. It was purified by recrystallization from 50% ethyl alcohol. Yield 3.5 g (76% of the theoretical). The cream-colored powder melted at 248-249°; it dissolved in cold glacial acetic acid, hot ethyl alcohol, acetone and pyridine; insoluble in water, benzene, ether and chloroform.

5.264 mg substance: 13.32 ml 0.01 N H_2SO_4. 5.158 mg substance: 13.09 ml 0.01 N H_2SO_4. 7.688 mg substance: 4.580 mg AgCl. 8.203 mg substance: 4.805 mg AgCl. Found %: N 35.43, 35.53; Cl 14.74, 14.50. $C_9H_9N_6Cl$. Calculated %: N 35.52; Cl 15.01.

5. Formaldehyde-bisulfite derivative of 2-amino-4-(*p*-chloro-*m*-aminophenyl)-amino-1,3,5-triazine. A mixture of 5 g (1 mole) 2-amino-4-(*p*-chloro-*m*-aminophenyl)-amino-1,3,5-triazine, 3 g (1.05 moles) formaldehyde bisulfite compound, 50 ml alcohol and 5 ml water was heated with stirring at the boil for 20 hours. The precipitate was filtered off, washed with alcohol and recrystallized from water. Yield 3.5 g (46.9% of the theoretical). White powder, readily soluble in water, insoluble in organic solvents. Contains 1 mole of water of crystallization.

0.2078 g substance: 0.1283 g $BaSO_4$. Found %: S 8.47. $C_{10}H_{10}O_3N_6SNa \cdot H_2O$. Calculated %: S 8.63.

6. 2-Amino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-acetonitrile. 36.5 g N-(4-chlorophenyl)-biguanide (anhydrous with m.p. 128-129°) was dissolved in 120 ml absolute alcohol; to the solution was added 20 g ethylcyanoacetate. The mixture was heated at the boil in a flask under a reflux condenser for 2 hours. The yellow precipitate was filtered off, washed with alcohol and recrystallized from 50% alcohol. Yield 18 g (40% of the theoretical). Cream-colored plates with m.p. 225-226°, insoluble in water, soluble in alcohol and acetic acid.

5.014 mg substance: 11.44 ml 0.01 N H_2SO_4. 4.697 mg substance: 10.65 ml 0.01 N H_2SO_4.
Found %: N 31.94, 31.74. $C_{11}H_9N_6Cl$. Calculated %: N 32.24.

7. 2-Amino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-acetic acid. 10 g of the above-prepared 2-amino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-acetonitrile in 195 ml 16% aqueous NaOH was heated at the boil for 3 hours. The precipitate gradually went into solution. The solution was cooled, filtered from turbidity and neutralized with hydrochloric acid (1:1). The triazylacetic acid was purified through the sodium salt. Yield 9.6 g (90% of the theoretical). Cream-colored powder with m.p. 326-327°. Insoluble in water and organic solvents; soluble in weak acids and alkalies.

2.529 mg substance: 4.42 ml 0.01 N H_2SO_4. 2.113 mg substance: 3.72 ml 0.01 N H_2SO_4.
Found %: N 24.47, 24.67. $C_{11}H_{10}N_5O_2Cl$. Calculated %: N 25.04.

8. Ethyl ester of 2-isopropylamino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-propionic acid. To a mixture of 15 g N'-(4-chlorophenyl-N^5-isopropylbiguanide in 150 ml absolute toluene and 10.5 g anhydrous sodium carbonate was added dropwise, with energetic stirring, a solution of 13.5 g of the half ester acid chloride of succinic acid [13] in 100 ml absolute toluene at 65-70°. The temperature was gradually raised and was held at 110° for 20 hours (until disappearance of the biguanide reaction with ammoniacal copper sulfate solution). The solution was filtered hot from the precipitated sodium chloride. The filtrate solidified to a red-brown gel when cooled; it was carefully filtered from the toluene and to the residue was added weak hydrochloric acid and ether. With intense cooling, rubbing with a rod brought down crystals of the hydrochloride which were filtered off and repeatedly washed with ether. The hydrochloride was recrystallized from a mixture of 40 ml ethyl alcohol and 50 ml ether. Yield 10 g (50% of the theoretical). Needles with m.p. 165-166°, almost insoluble in water, insoluble in ether, soluble in alcohol.

4.163 mg substance: 7.914 mg CO_2; 2.207 mg H_2O. 3.584 mg substance: 4.47 ml 0.01 N H_2SO_4.
3.052 mg substance: 3.82 ml 0.01 N H_2SO_4. Found %: C 51.88; H 5.93; N 17.46, 17.59.
$C_{17}H_{22}O_2N_5Cl \cdot HCl$. Calculated %: C 50.99; H 5.75; N 17.50.

The ethyl ester of 2-isopropylamino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-propionic acid was isolated in the free state by treatment of the aqueous suspension of the hydrochloride with 17% NaOH solution in presence of ether. The mixture was shaken until the precipitate dissolved completely. The ether layer was separated and the ether distilled off. The residual oil was recrystallized from a little alcohol. Thin plates with m.p. 86-90°. Readily soluble in alcohol and ether; insoluble in water.

3.260 mg substance: 6.669 mg CO_2; 1.817 mg H_2O. 3.205 mg substance: 6.600 mg CO_2; 1.722 mg H_2O.
3.619 mg substance: 4.93 ml 0.01 N H_2SO_4. Found %: C 55.82, 56.19; H 6.23, 6.01; N 19.07.
$C_{17}H_{22}O_2N_5Cl$. Calculated %: C 56.12; H 6.05; N 19.25.

9. 2-Isopropylamino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-propionic acid. 3.75 g ethyl ester of 2-isopropylamino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-propionic acid hydrochloride was dissolved in 15 ml warm absolute alcohol, and to the solution was added 20 ml 4% alcoholic solution of NaOH. The precipitated sodium chloride was filtered off. The solution was heated on the water bath at the boiling point of alcohol for half an hour. The precipitate was filtered off and dissolved in 30 ml water, and the pure solution was acidified with dilute hydrochloric acid to a pH of 2. On standing, the precipitated gel formed crystals which were filtered off, dissolved in sodium bicarbonate solution and reprecipitated with dilute hydrochloric acid. The triazylpropionic acid was recrystallized from 30 times the amount of alcohol. Yield 2 g (63.7% of the theoretical). Needles with m.p. 216-218°, insoluble in water and acids; sparingly soluble in alcohol; soluble in bicarbonate solution.

0.1165 g substance: 3.51 ml 0.1 N NaOH. Calculated: 3.47 ml 0.1 N NaOH. 4.507 mg substance: 8.880 mg CO_2; 2.138 mg H_2O. 4.323 mg substance: 8.541 mg CO_2; 2.109 mg H_2O. 4.160 mg substance: 6.30 ml 0.01 N H_2SO_4. Found %: C 53.77, 53.92; H 5.31, 5.46; N 21.20. $C_{15}H_{18}O_2N_5Cl$. Calculated %: C 53.65; H 5.36; N 20.86.

10. 2-Isopropylamino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-propionic acid hydrazide. 2.3 g ethyl ester of 2-isopropylamino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-propionic acid hydrochloride was dissolved in 7 ml absolute alcohol, and to the solution was added 2 ml hydrazine hydrate. The solution was heated at the boil for an hour and left for 24 hours. The precipitate was filtered off, washed with alcohol and ether and recrystallized from 75% alcohol. Yield 1.7 g (85% of the theoretical). Needles, m.p. 168-170°. Insoluble in water and ether; soluble in alcohol.

4.219 mg substance: 7.950 mg CO_2; 2.110 mg H_2O. 1.698 mg substance: 3.40 ml 0.01 N H_2SO_4. 1.801 mg substance: 3.60 ml 0.01 N H_2SO_4. Found %: C 51.42; H 5.59; N 28.02, 27.98. $C_{15}H_{20}ON_7Cl$. Calculated %: C 51.50; H 5.72; N 28.04.

SUMMARY

1. A series of 2,4-diamino-1,3,5-triazine derivatives was prepared by cyclization of the corresponding biguanide derivatives with esters of monobasic acids and the monoacid chlorides of dibasic acid half-esters. The latter method permitted direct preparation of the ester of a substituted 2,4-diamino-1,3,5-triazyl-6-alkylcarboxylic acid.

2. The following were synthesized: N-(4-chloro-3-nitrophenyl)-biguanide; 2-amino-4-(p-chloro-m-nitrophenyl)-amino-1,3,5-triazine; 2-amino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-acetonitrile; the ethyl ester and hydrazide of 2-isopropyl-amino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-propionic acid; 2,4-diamino-4-(p-chloro-m-aminophenyl)-amino-1,3,5-triazine, its formaldehyde-bisulfite derivative and its hydrochloride; 2-amino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-acetic acid; 2-isopropylamino-4-(p-chlorophenyl)-amino-1,3,5-triazyl-6-propionic acid.

The last four compounds proved to be inactive when tested for antimalarial action.

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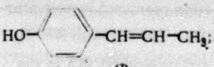
THE PROBLEM OF THE ESTROGENIC ACTIVITY OF ANOL DIMERS

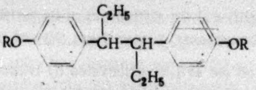
II. SYNTHESIS OF THE ISOMERIC 3,5-DI-(p-HYDROXYPHENYL)-4-METHYLPENTENES

O. S. Madaeva, N. M. Goncharova and V. I. Maksimov

We have reported [1] that anol – p-propenylphenol (I) – is capable of transformation in various conditions into compounds possessing the properties of the male sexual hormone. It was shown that the liquid mixture of polymers formed on lengthy standing of the pure anol has an estrogenic activity of the order of 1γ; that from the mixture of substances formed on demethylation of anethole with potassium hydroxide at 200-220° can be isolated a fraction that stimulates estrus in mice in a dose of 0.1-1γ; and that a fraction with the same activity was obtained by vacuum-distillation of the resinous substances obtained by 2 hours' heating of anol at 230°.



(I)



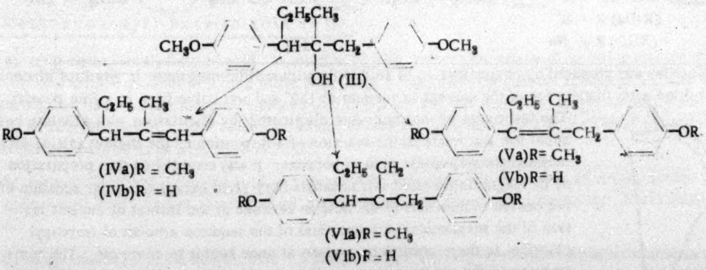
(IIa) R= H

(IIb) R = CH_3

We rejected the statements of Dodds and co-workers [2] that the estrogenic properties of compounds prepared by demethylation of anethole with potassium hydroxide are due to the presence in them of meso-3,4-di-(p-hydroxyphenyl)hexane (synestrol, IIa), and evidence was presented that the high estrogenic activity of substances formed from anol is due to some of its dimers – isomers of 3,5-di-(p-hydroxyphenyl)-4-methylpentenes. One of these dimers of anol – Δ_4–3,5-di-(p-hydroxyphenyl)-4-methylpentene (IV b) – was isolated by us from a mixture of polymers of anol in the pure crystalline form.

In further work on the fractionation of mixtures formed by polymerization of anol and on the separation from them of pure compounds, difficulties were encountered. We were unable to overcome these difficulties, and we therefore decided to attempt the synthetic preparation of the anol dimers of interest to us.

In this paper we describe an investigation of the dehydration of 3,5-di-(p-methoxyphenyl)-4-methylpentan-4-ol (III) and the preparation therefrom of the unsaturated compounds (IVa), (Va) and (VIa); we also studied the corresponding phenols (IVb), (Vb) and (VIb):



(III)

(IVa)R = CH_3

(IVb)R = H

(Va)R= CH_3

(Vb)R= H

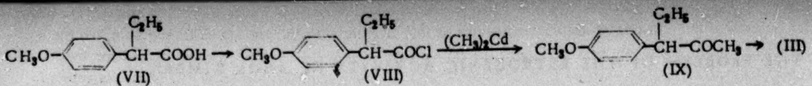
(VIa)R = CH_3

(VIb)R = H

Two methods were used for preparation of the starting carbinol (III). In both of these we started from α-(p-methoxyphenyl)-butyric acid (VII), prepared from α-(phenyl)-butyric acid via p-nitro-, p-amino and p-hydroxy-α-(phenyl)-butyric acid and methylation of the phenolic hydroxyl group of the latter with dimethyl sulfate.

In the first variant we attempted to prepare the carbinol (III) by the action of 3-(p-methoxyphenyl)-pentan-4-one [3] (IX) on p-methoxybenzyl magnesium bromide.

The ketone (IX) was synthesized by us from α-(p-methoxyphenyl)-butyryl chloride (VIII) and dimethylcadmium in 82.5% yield.



However, the reaction of p-methoxybenzyl magnesium bromide with (IX) does not proceed smoothly and carbinol (III) is formed in insignificant yield, in addition to which it is badly contaminated with dianisyl (side-product of the reaction of p-methoxybenzyl bromide with magnesium). This variant could not, therefore, be applied for preparative purposes. The prepared carbinol (III) was dehydrated by heating with iodine in xylene solution; oxidation of the formed mixture of unsaturated compounds with potassium permanganate in acetone [4] gave anisic acid; the neutral fraction of the oxidation products yielded a semicarbazone with m.p. 189° which did not depress the m.p. of 3-(p-methoxyphenyl)-pentan-4-one (IX) semicarbazone, which we also prepared by oxidation of isoanethole (IVa).

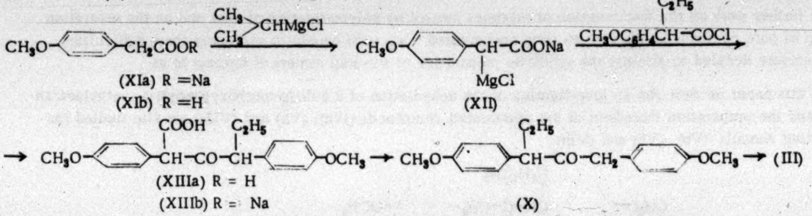
Formation of anisic acid and of ketone (IX) indicates that the main product of dehydration of carbinol (III) in these conditions was isoanethole (IVa).

The unsatisfactory yield of carbinol (III) and the difficulties of its purification prompted us to synthesize it by the other route from 3,5-di-(p-methoxyphenyl)-pentan-4-one (X) and methyl magnesium bromide.

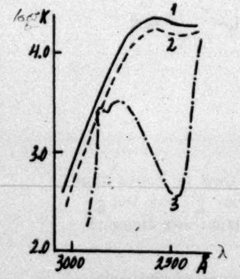
For the preparation of (X) we exploited the ability (discovered by Ivanov and co-workers [5]) of the sodium salt of phenylacetic acid to react with isopropyl magnesium bromide with formation of propane and the α-magnesium chloride derivative of phenylacetic acid.

The authors utilized this property for a series of reactions, including the preparation of alkylaromatic ketones.

We extended this reaction to the sodium salt of α-(p-methoxyphenyl)-acetic acid (XIa), and the synthesis of ketone (X) was performed according to the scheme:



The sodium salt (XIa) was prepared by neutralization of acid (XIb) with sodium carbonate in absolute alcohol solution; it was dried after distillation of the solvent in vacuum at 130° and was pulverized to a fine powder. The last traces of moisture were eliminated by distillation with absolute benzene; use was made in the reaction of a suspension of the sodium salt of α-(p-methoxyphenyl)-acetic acid in benzene. It was established that preparation of its magnesium halide salt in satisfactory yield necessitated the addition of the heated sodium salt of the acid in benzene at the instant of violent reaction of the magnesium with one-third of the required amount of isopropyl chloride; in these conditions propane at once begins to come off. The temperature of the reaction mass was held at 60° during addition of the remaining amount of isopropyl chloride, as well as afterwards until no more propane came off.



1 - Isoanethole; 2 - mixture of isomers; 3 - synestrol dimethyl ether.

The condensation of (XII) with α-(p-methoxyphenyl)-butyryl chloride (VIII) and the subsequent decarboxylation of the keto acid (XIIIa) proceed smoothly and lead to the formation of 3,5-di-(p-methoxyphenyl)-pentan-4-one (X) in 48% yield. Reaction of (X) with methyl magnesium bromide gives a 98% yield of 3,5-di-(p-methoxyphenyl)-4-methylpentan-4-ol (III).

We effected the dehydration of the tertiary carbinol (III) by the method of A.P. Orekhov — boiling with acetyl chloride. The obtained mixture of 3,5-di-(p-methoxyphenyl)-4-methylpentenes was an oily, noncrystallizing mass.

Comparison of the ultraviolet absorption spectra of this mixture with the spectra of isoanethole and the dimethyl ether of synestrol (IIb) showed that the mixture does not contain isomer (VIa) [whose absorption spectrum must be of the same order as that of (IIb)]. Moreover, the possibility of formation of this isomer is very remote because A. P. Orekhov and co-workers [6, 7, 8] had shown that in the dehydration of tertiary carbinols of this series, the double bond is formed by cleavage of hydrogen from the less readily hydrogenated atom of carbon situated in the α-position to the phenyl radical.

The absorption spectrum of the prepared mixture (see diagram on previous page) was very similar to the absorption spectrum of isoanethole (IVa).

Oxidation of the mixture of 3,5-di-(p-methoxyphenyl)-4-methylpentenes in the conditions described for the oxidation of isoanethole [9] yielded, as main products, anisic acid and (from the neutral fraction) the semicarbazone of 3-(p-methoxyphenyl)-pentan-4-one (IX). From the recrystallization mother liquors of this semicarbazone was obtained only a very small quantity of a mixture of other semicarbazones. Evidently the dehydration of (III) leads mainly to formation of isoanethole (IVa).

Demethylation of the obtained mixture of unsaturated compounds with an alcoholic solution of KOH at 225-230° gave a light-yellow, resinous substance distilling at 190-193° (0.3 mm). On addition of benzene it partly crystallized. After recrystallization from benzene the precipitated product melted at 98-99° and did not give a depression with $\Delta_{4,5}$-3,5-di-(p-hydroxyphenyl)-4-methylpentene (IVb) prepared by demethylation of isoanethole in the same conditions. Its p-nitrobenzoate likewise did not give a depression with isoanol p-nitrobenzoate (m.p. 164°).

After separation of crystalline isoanol from the oily residue, which was undoubtedly a mixture, we were unable to isolate the individual substances.

Biological tests on the prepared mixture of 3,5-di-(p-hydroxyphenyl)-4-methylpentenes showed that it was capable of starting estrus in young mice after three injections under the skin in doses of up to 0.5γ in solution in peach oil. A most interesting and important fact is that the filtrate after separation of the crystalline isoanol (IVb) possessed an estrogenic activity of the order of 0.125-0.5γ. Isoanol (IVb), as we know, develops estrogenic activity only in doses of 100γ. Such a high activity of the obtained synthetic mixture of anol dimers — derivatives of 3,5-di-(p-hydroxyphenyl)-4-methylpentenes — confirms our previously expressed opinion that the latter are actually the cause of the estrogenic properties of the products of polymerization of anol.

EXPERIMENTAL

α-(p-Methoxyphenyl)-butyric acid (VII).

a) α-(p-Nitrophenyl)-butyric acid. A solution of 50 g α-phenylbutyric acid in 336 g sulfuric acid (sp. gr. 1.84) is nitrated with a mixture of 27.8 g nitric acid (sp.gr. 1.52) and 38.7 g sulfuric acid (sp. gr. 1.84) at +5°. On the following day the reaction mixture is poured into 305 g ice and the separated α-(p-nitrophenyl)-butyric acid is purified by recrystallization from twice the weight of 50% acetic acid. Yield 36 g (50% of the theoretical) of α-(p-nitrophenyl)-butyric acid with m.p. 120-122°.

b) α-(p-Aminophenyl)-butyric acid was prepared by reduction with hydrogen of α-(p-nitrophenyl)-butyric acid in presence of Raney nickel catalyst at 80° and an initial pressure of 30 atmospheres. Yield 78.3%, m.p. 138.5-140°

c) α-(p-Hydroxyphenyl)-butyric acid. A solution of 35.8 g α-(p-aminophenyl)-butyric acid in a mixture of 58.8 g sulfuric acid (sp. gr. 1.84) and 160 ml water is diazotized with a solution of 15.2 g sodium nitrite in 40 ml water at +5°. The diazonium salt is decomposed by introducing it into a boiling solution of 720 g 8% sulfuric acid. Yield of α-(p-hydroxyphenyl)-butyric acid with m.p. 127-128° is 77.8% of the theoretical.

d) α-(p-Methoxyphenyl)-butyric acid (VII) was prepared by methylation of α-(p-hydroxyphenyl)-butyric acid with dimethyl sulfate in the conditions of Wilds and Biggerstoff [9], m.p. 65-67° after recrystallization from petroleum ether; yield 94% of theory.

p-Methoxyphenylacetic acid (XIb) is prepared from phenylacetonitrile through p-nitrobenzyl cyanide and p-nitrophenylacetic acid. Catalytic hydrogenation of the latter gives p-aminophenylacetic acid; this is diazotized and by the method of Carter and Hey [10] it is transformed into p-hydroxyphenylacetic acid which is methylated with dimethyl sulfate in the conditions described for compound (VII); (p-methoxyphenyl)-acetic acid melts at 83.5-84°.

3-(p-Methoxyphenyl)-pentan-4-one (IX)

α-(p-Methoxyphenyl)-butyryl chloride (VIII) was prepared by reaction of a benzene solution of α-(p-methoxyphenyl)-butyric acid with thionyl chloride. B.p. 133-135° at 10 mm.

A solution of methyl magnesium bromide is prepared from 4.8 g (0.2 mole) magnesium, 100 ml anhydrous ether and methyl bromide in a three-necked, round-bottomed flask of 250 ml capacity fitted with a reflux condenser, a stirrer, a mercury seal and a tube for passing through methyl bromide. Dimethylcadmium was prepared by rapidly adding to the ice-cooled methyl magnesium bromide solution 29.9 g (0.11 mole) cadmium bromide previously dehydrated by heating in a vacuum at 180-210° in a CO_2 stream. Stirring was then continued at room temperature until complete disappearance of the methyl magnesium bromide (negative reaction with Michler's ketone). To the formed organocadmium compound is added dropwise 21.2 g (0.1 mole) α-(p-methoxyphenyl)-butyryl chloride at such a speed that the reaction mass boils. After the whole of the chloride has been added, the mixture is heated for an hour at 40°. On the following day the reaction mass is decomposed with 5% sulfuric acid solution while cooling. The ethereal solution is separated and the aqueous layer is extracted with ether. The combined ether extracts are washed with 5% NaOH solution and dried with sodium sulfate; the solvent is distilled off. The residual oil is distilled in vacuum to give a fraction with b.p. 87-88° at 0.4 mm. Yield 82.4%. The semicarbazone, prepared by digesting (IX) with a solution of semicarbazide acetate, formed rhombic platelets (from alcohol), m.p. 187-188° (the literature gives 188-189° [3]).

The presence of a ketone group and the high degree of purity of the prepared ketone were established by determination of the oxime number by titration in presence of bromophenol blue. After the ketone had been boiled with hydroxylamine hydrochloride, the amount of released hydrochloric acid exactly corresponded to the weight of the ketone sample.

Determinations of nitrogen in the liquid oxime gave the following results:

8.525 mg substance: 0.332 ml N_2 (23°, 730 mm). Found %: N 4.32. $C_{19}H_{23}O_3N$. Calculated %: N 4.36.

3,5-Di-(p-Methoxyphenyl)-pentan-4-one (X)

a) Anhydrous sodium salt of (p-methoxyphenyl)-acetic acid. An alcoholic solution of 17.7 g (p-methoxyphenyl)-acetic acid is neutralized with 5.71 g sodium carbonate with heating. The solvent is evaporated in vacuum and the dry, hygroscopic residue of the sodium salt is finely pulverized and dried in a vacuum drying cupboard at 130°. The last traces of moisture are removed from the sodium salt by mixing with 60 ml absolute benzene and distilling off 30 ml benzene from the mixture.

b) 3,5-Di-(p-methoxyphenyl)-pentan-4-one is prepared in an apparatus consisting of a 250 ml three-necked flask fitted with a reflux condenser, stirrer, mercury seal and dropping funnel. The condenser is connected, via phosphorus pentoxide drying bottles, with a measuring cylinder filled with water for trapping the propane. To 4.43 g (0.184 mole) magnesium in 40 ml absolute ether is added a crystal of iodine and 1.73 g freshly distilled isopropyl chloride. After the start of the reaction, addition is made to the mixture of 80 ml absolute ether and (dropwise) 3.86 g isopropyl chloride; into the boiling reaction mass is rapidly introduced 20 g (0.106 mole) sodium (p-methoxyphenyl)-acetate in benzene. The bath temperature is raised to 55-60°; vigorous evolution of propane then commences and the gas is collected in the measuring cylinder. As soon as the gas evolution slows down, addition is made to the reaction mass of a further 8.76 g isopropyl chloride in 45 ml absolute ether over a period of $1\frac{1}{2}$ - 2 hours. Heating at the specified temperature is continued until propane ceases to come off. If these conditions are observed, the magnesium halide complex is formed in a yield of about 70%, judging by the volume of propane collected. To the so-prepared reaction mass, containing the sodium salt of the magnesium halide compound of (p-methoxyphenyl)-acetic acid (XII), is added dropwise, while cooling with ice water and stirring, 22.47 g (0.106 mole) freshly distilled α-(p-methoxyphenyl)-butyryl chloride. Heat is developed. The mixture is boiled on the water bath for 3 hours. The resultant complex is decomposed by a 25% solution of ammonium chloride while being cooled. The resultant sodium salt of the ketocarboxylic acid (XIIIb) is decarboxylated by acidifying the reaction mass with sulfuric acid (acid reaction to Congo) and heating to boiling on the water bath for 2 hours. The ethereal solution is separated while cooling, and the aqueous layer is extracted with ether. The ether extracts are washed with 10% potassium hydroxide solution and with water and then dried with sodium sulfate; the solvent is then distilled off. Yield 22.2 g oily product. This is distilled in vacuum to give a fraction at 187-200° (2 mm). It partly crystallizes after standing for a long time in a refrigerator. The crystals are filtered, washed with alcohol and petroleum ether.

After recrystallization from alcohol, the m.p. is 51-52°; the yield of 3,5-di-(p-methoxyphenyl)-pentan-4-one is 47.8% of the theoretical.

3.35 mg substance: 9.336 mg CO_2; 2.168 mg H_2O. Found %: C 76.58; H 7.29.
$C_{19}H_{22}O_3$. Calculated %: C 76.46; H 7.43.

This ketone does not give crystalline derivatives either with semicarbazone, hydroxylamine or m-dinitrophenylhydrazone.

3,5-Di-(p-Methoxyphenyl)-4-methylpentan-4-ol (III)

To an ice-cooled solution of methyl magnesium bromide, prepared from 1.17 g (0.049 mole) magnesium in 12 ml absolute ether, is added dropwise with stirring a solution of 5 g (0.017 mole), 3,5-di-(p-methoxyphenyl)-pentan-4-one in 30 ml absolute ether. The reaction mass is then boiled on the water bath for 2 hours. On the following day decomposition of the organomagnesium complex is effected under cooling with 25% ammonium chloride solution. After acidification with 20% sulfuric acid solution (to Congo), the aqueous layer is extracted with ether. The ether extracts are washed with water and dried with sodium sulfate and the ether is distilled off. Yield 5.1 g (98% of theory), of carbinol (III).

4.029 mg substance: 11.317 mg CO_2; 2.996 mg H_2O. Found %: C 76.60; H 8.31.
$C_{20}H_{26}O_3$. Calculated %: C 76.38; H 8.33.

7.871 mg substance: 0.63 ml CH_4 (16.5°, 733 mm). Found %: OH 5.56. $C_{20}H_{26}O_3$.
Calculated %: OH 5.41.

Dehydration of 3,5-di-(p-methoxyphenyl)-4-methylpentan-4-ol

5.1 g 3,5-di-(p-methoxyphenyl)-4-methylpentan-4-ol is heated with 4.7 g freshly distilled acetyl chloride on a water bath under a reflux condenser and calcium chloride tube until hydrogen chloride ceases to come off. The mixture is then poured on to ice and carefully neutralized with 10% NaOH solution. The separated oil is extracted with ether and the extract washed with water, dried with calcium chloride and distilled to remove the solvent. Vacuum fractionation of the oily residue (4.75 g), gave 3.4 g (71.5% of theory), of a light-yellow, mobile liquid with b.p. 186-187° at 0.6 mm. Its elementary analysis is consistent with a dimer of anol.

3.191 mg substance: 9.476 mg CO_2; 2.327 mg H_2O. Found %: C 80.99; H 8.16. $C_{20}H_{24}O_2$.
Calculated %: C 81.03; H 8.16.

Oxidation of the products of dehydration of carbinol (III)

0.82 g of the substance with b.p. 186-187° at 0.6 mm was oxidized with potassium permanganate in acetone solution in the conditions described for the oxidation of isoanethole. 40% (0.32 g) of the starting substance was recovered unchanged. From the acid fraction of the oxidation products was separated a precipitate with m.p. 177-178° which did not give a depression with anisic acid (m.p. 179-180°). Treatment of the neutral products of oxidation with a solution of semicarbazide acetate gave a mixture of semicarbazones with m.p. 171.5-172°. After several recrystallizations from alcohol and benzene, a semicarbazone was isolated with m.p. 189° which did not give a depression with the semicarbazone of 3-(p-methoxyphenyl)-pentan-4-one prepared by oxidation of isoanethole.

Demethylation of products of dehydration of carbinol (III)

7.6 g potassium hydroxide, 3.4 g dehydration products of carbinol (III) and 19 g methanol are heated in an experimental autoclave at 225-230° for 24 hours. 10 ml methanol is then distilled off from the reaction mass, and to the residue is added 10 ml water with which the methanol residues are completely distilled off. The oily substance which separated from the aqueous-alkaline solution was extracted with ether. The aqueous-alkaline solution was diluted with 40 ml water prior to acidification with 20% sulfuric acid solution (to Congo). The resultant oil was extracted with ether; after the usual working-up and the distillation of the ether, 1.95 g of a mixture of 3,5-di-(p-hydroxyphenyl)-4-methylpentenes (IVb, Vb, VIb) was obtained. Vacuum distillation gave a fraction with b.p. 190-193° at 0.2 mm. Yield 1 g.

5.153 mg substance: 15.174 mg CO_2; 3.492 mg H_2O. Found %: C 80.31; H 7.58.
$C_{18}H_{20}O_2$. Calculated %: C 80.55; H 7.51.

On treating 0.6 g of the obtained fraction with benzene in the cold, it partly crystallized to give 0.15 g crystals. After repeated recrystallization from benzene, the m.p. was 98-99°; the substance does not give a depression with 3,5-di-(p-hydroxyphenyl)-4-methylpentene (IVb) previously obtained by demethylation of isoanethole. The p-nitrobenzoate of this crystalline precipitate likewise does not depress the melting point of isoanol p-nitrobenzoate (m.p. 164°).

SUMMARY

1. The dehydration of 3,5-di-(p-methoxyphenyl)-4-methylpentan-4-ol was investigated.

2. A mixture of dimers of anol – isomeric 3,5-di-(p-hydroxyphenyl)-4-methylpentenes – was prepared by a synthetic route.

3. The structure of isoanol was confirmed by synthesis as $\Delta_{4,5}$-3,5-di-(p-hydroxyphenyl)-4-methylpentene.

4. It is shown that the prepared mixture of isomers of 3,5-di-(p-hydroxyphenyl)-4-methylpentene possesses a high estrogenic activity.

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THE DIPOLE MOMENTS OF SOME FURAN AND THIOPHENE DERIVATIVES

L. M. Nazarova and Ya. K. Syrkin

Following on our previously published [1] measurements of the dipole moments of some compounds of the furan and thiophene groups, we have now measured the dipole moments of 2-bromothiophene, 2,5-dibromothiophene, 5-bromo-2-nitrofuran and 5-nitro-2-furaldehyde.

All the measurements were made in benzene at 25° by the heterodyne method in an apparatus permitting simultaneous determination of the dielectric constant and the density of the solution.

The results of the measurements are presented in Table 1, where P_∞ is the total polarization at infinite dilution; R_D is the molar refraction for the sodium D line, calculated additively in cases 2, 3, and 4 and found experimentally for 2-bromothiophene; μ is the dipole moment.

TABLE 1

No.	Substance	P_∞	R_D	$\mu \cdot 10^{18}$
1	2-Bromothiophene	72.34	33.62	1.36
2	2,5-Dibromothiophene	65.50	41.30	1.08
3	5-Bromo-2-nitrofuran	391.86	32.66	4.17
4	5-Nitro-2-furaldehyde	273.64	31.96	3.42

EXPERIMENTAL

We synthesized the investigated compounds by the literature methods. Purification of the solid compounds was effected by recrystallization until the melting points were constant. The liquid compounds were purified by repeated vacuum distillation. Dibromothiophene was synthesized twice and purified by two methods: five distillations in vacuum and conversion to the mercury compound which was fractionally crystallized from dioxane. The dibromothiophene then separating from the appropriate fraction was distilled in vacuum. The dipole moments of both specimens were measured and found to be identical.

The compounds had the following characteristics:

Benzene: Freezing point +5.5°; b.p. 80.12° ±0.01 at 760 mm.

2-Bromothiophene: B.p. 38.8-39.5° at 13.5 mm (the whole of the thread of the thermometer was immersed in the vapor); d_{20}^{20} 1.6284; n_D^{20} 1.5865; MR_D 33.62.

2,5-Dibromothiophene: B.p. 56.5° at 1.5 mm (whole of thread in vapor). Freezes in dry ice and melts at − 6°.

5-Bromo-2-nitrofuran: was recrystallized from petroleum ether; m.p. 48.0-48.35° (corr.).

5-Nitro-2-furaldehyde: was recrystallized from benzene, m.p. 34.6-35.1° (corr.).

The dielectric constants were measured in benzene at 25°. The total polarization was calculated by the method of Hödestrand [2]. Results are set out in Tables 2 to 5 where m denotes the concentration of the substance expressed in molar percentrages; d is the density of the solution; ϵ is the dielectric constant. A, B, α and β are constants calculated by Hödestrand's method.

TABLE 2

2-Bromothiophene				2-Bromothiophene			
No.	m	d	ϵ	No.	m	d	ϵ
0	0	0.87271	2.2714	0	0	0.87255	2.2714
1	0.3736	0.87601	2.2831	1	0.2771	0.87507	—
2	0.7559	0.87936	2.2927	2	0.3600	0.87581	2.2823
3	1.1303	0.88264	2.3042	3	0.5200	0.87710	2.2870
4	1.4988	0.88604	2.3155	4	0.6879	0.87877	2.2924
5	1.8567	0.88930	2.3263	5	0.8694	0.88032	2.2982
Extrap.	(1.9000)	(0.88960)	(2.3300)	Extrap.	(1.0000)	(0.88156)	(2.3020)

A = 0.34106; B = 14.7059; α = 2.93; β = 0.889; P_∞ = 71.00

A = 0.34110; B = 14.7087; α = 3.06; β = 0.901; P_∞ = 73.11

Average P_∞ = 72.34

EVALUATION OF RESULTS

On comparing our experimental values for the dipole moments with the corresponding vectorial sums of the bond moments, we see that in the case of 2-bromothiophene ($\mu_{vect.}$ = 2.20) and 2,5-dibromothiophene ($\mu_{vect.}$ = 1.40) the moments are low, as had already been observed for 2-bromofuran and 2,5-dibromofuran [1].

TABLE 3

2,5-Dibromothiophene purified by distillation				2,5-Dibromothiophene purified through the mercury derivative			
No.	m	d	ε	No.	m	d	ε
0	0	0.87284	2.2714	0	0	0.87280	2.2714
1	0.0852	0.87419	2.2736	1	0.0820	0.87394	2.2733
2	0.3108	0.87781	2.2781	2	0.3149	0.87767	2.2781
3	0.4856	0.88068	2.2817	3	0.4859	0.88040	2.2815
4	0.6435	0.88312	2.2849	4	0.6633	0.88327	2.2852
5	0.8310	0.88608	2.2887	Extrap.	(1.0000)	(0.88861)	(2.2928)
Extrap.	(1.0000)	(0.88876)	(2.2929)				

A = 0.34101; B = 14.7037;
α = 2.150; β = 1.592;
P_∞ = 65.56.

A = 0.34107; B = 14.7061;
α = 2.140; β = 1.591;
P_∞ = 65.45

Average: P_∞ = 65.50

TABLE 4

5-Bromo-2-nitrofuran			
No.	m	d	ε
0	0	0.87266	2.2714
1	0.1793	0.87468	2.3150
2	0.2832	0.87587	2.3406
3	0.4114	0.87737	2.3721
4	0.5285	0.87877	2.4010
5	0.6631	0.88029	2.4342
Extrap.	(1.0000)	(0.88426)	(2.5174)

A = 0.34108; B = 14.7067;
α = 24.60; β = 1.160;
P_∞ = 391.86.

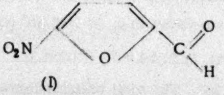
TABLE 5

5-Nitro-2-furaldehyde					
No.	m	d	ε	α	β
0	0	0.87273	2.2714	16.65	0.633
1	0.1201	0.87355	2.2915	16.74	0.633
2	0.2694	0.87443	2.3171	16.96	0.631
3	0.4201	0.87542	2.3432	17.09	0.640
4	0.5266	0.87604	2.3620	17.20	0.629

A = 34106. B = 14.7056.
P_∞ = 273.64.

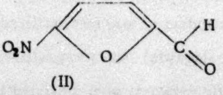
The moment of 5-bromo-2-nitrofuran is found to have a considerable exaltation ($\mu_{vect.}$ = 2.72, a difference of 1.45), i.e., in this case also, the nitro group brings about a considerable increase of the moment.

For nitrofuraldehyde the vector sums were calculated for two different positions of the carbonyl group:



(I)

and



(II)

In the case of (I) the vector sum is 1.11 D; in case (II) it is 4.31 D. The magnitude of the moment obtained by measurement (3.42 D) shows that internal rotation is here possible.

In all cases the vector sums were calculated with magnitudes of bond moments taken from aliphatic derivatives: μ_{C-Br} = 2.00 D; μ_{NO_2} = 3.40D; μ_{C-O} = 2.70 D. The moment of thiophene is 0.60 D; the moment of furan is 0.71 D. The angle at which the vectors are inclined to the ring moment is 78.5° for thiophene and 72° for furan.

SUMMARY

1. The dipole moments were measured of 2-bromothiophene (1.36 D), 2,5-dibromothiophene (1.08 D), 5-bromo-2-nitrofuran (4.17 D) and 5-nitro-2-furaldehyde (3.42 D).

2. The obtained magnitudes of the dipole moments were compared with the corresponding vector sums of the bond moments.

3. It is noteworthy that the dipole moments of bromo derivatives of thiophene are low in comparison with the

vector sum. The same observation was made for bromo derivatives of furan. The moment of 2-bromo-5-nitrofuran is low in relation to the vector sum. Internal rotation is possible in the case of 5-nitrofuraldehyde.

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REACTION OF QUATERNARY SALTS OF HETEROCYCLIC BASES WITH AROMATIC NITROCHLORO COMPOUNDS

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A. I. Kiprianov and F. S. Babichev [1,2] found that methine bases of the thiazole series differ from the methine bases of other hetercyclic nitrogen compounds in reacting with alkyl halides, α-halodiketones and acid chlorides.

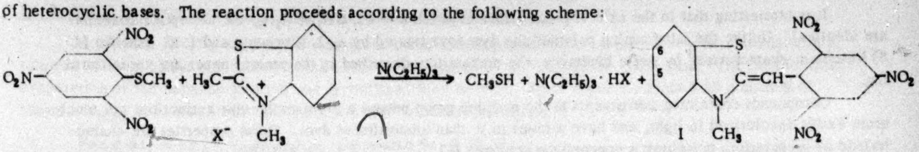
We were interested in establishing how methine bases of the thiazole series would react with picryl chloride and similar compounds.

Wizinger and Coenen [3] investigated the reaction of aromatic nitrochloro compounds with methine bases of the pseudoindole and quinaldine series. The reaction was performed by heating a mixture of the benzene solutions of the methine base and the aromatic nitrochloro compound and proceeded with formation of a deeply colored product; only half of the methine base enters into the condensation, the other half forming a quaternary salt.

We synthesized preparations 1 to 6 (see Experimental) and found that methine bases of the thiazole series react with picryl chloride in the above-described conditions in a similar manner to the quinaldine bases.

For the synthesis of such dyes, however, it is much more convenient to take the quaternary salt and to conduct the reaction in a medium of absolute alcohol in presence of triethylamine. In the majority of cases the dyes are then separated in the crystalline form. Yields for derivatives of thiazole and benzothiazole reach 80-90% of the theoretical.

Methylpicryl sulfide and trinitroanisole also enter into the condensation reaction with quaternary salts of heterocyclic bases. The reaction proceeds according to the following scheme:



The yields of dyes (I) in this reaction likewise reach 80-90% of the theoretical.

TABLE 1

I. R	Position of substituent	λ_{max} (in mμ) in benzene
H	–	552
NO_2	6	533
$N(CH_3)_2$	6	599
OCH_3	5	560
CF_3.	5	535

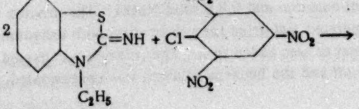
TABLE 2

IV. R	R'	$\lambda_{max.}$ (in mμ) in benzene	$E \cdot 10^{-4}$
CH_3	H	552	3
C_6H_5	H	554	–
CH_3	CH_3	605	1.25
CH_3	C_2H_5	605	–
C_2H_5	Cl	605	–
C_2H_5	CH_3	610	–

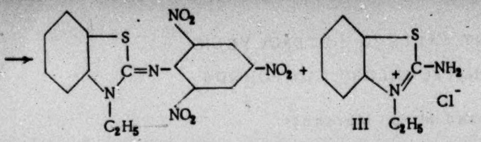
Applying these methods, we synthesized a series of preparations containing various substituents in the benzene ring of benzothiazole. Introduction of electropositive substituents brings about a shift of the absorption maximum in the direction of long waves, while electronegative substituents cause a shift in the short-wave direction. This is seen from Table 1.

In addition to picryl chloride, we condensed dinitrochlorobenzene and 3,5-dinitro-4-chlorobenzotrifluoride with 3-methyl-2-methylenebenzothiazoline. The absorption maxima of the dyes prepared from these compounds (see Experimental, preparations 4 and 5) are shifted in the short-wave direction by comparison with the preparation derived from picryl chloride.

N-Ethylbenzothiazoloneimine (II) reacts with picryl chloride in a similar manner to the methine bases:



II



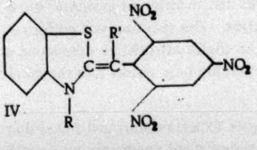
III

The absorption maximum of the dye (III) so obtained is shifted 100 mμ in the direction of the short waves in relation to preparation I.

Wizinger and Coenen [3] observe that methine bases containing substituents in the methylene group are incapable of reaction with picryl chloride.

We found, however, that methine bases and quaternary salts of 2-ethylbenzothiazole and 2-ethylbenzoselenazole react with picryl chloride. Also capable of condensation with picryl chloride are quaternary salts of 2-chloromethyl- and 2-n-propylbenzothiazole.

It is interesting that the resultant preparations (IV):



IV

have a considerably deeper color than compounds in which R'=H, as shown in Table 2.

Preparations in which R'=H have a reddish-violet color; replacement of the hydrogen of the methine group by CH_3, C_2H_5 and Cl leads to compounds with a dark-blue color.

The cause of such a sharp color change of the dyes is evidently the development of steric hindrances which make the molecules of the dye noncoplanar.

It is interesting that in the case of preparations in which R' = Cl, CH_3 or C_2H_5, the absorption maxima are identical. Unlike the salt-forming polymethine dyes investigated by A. I. Kiprianov and I. K. Ushenko [4, 5] which are characterized by steric hindrance, the preparations described in the present paper are nonsaltforming.

Compounds containing substituents in the methine group possess a lower molecular extinction, are much more easily decolorized in light, and have a lower m.p. than unsubstituted dyes. These properties are characteristic of preparations possessing a noncoplanar structure [6].

The authors express their profound thanks to Prof. A. I. Kiprianov for valuable observations and advice.

EXPERIMENTAL

2-Chloromethylbenzothiazole ethochloride

A solution of 3 g N-ethyl-o-aminothiophenol in 5 ml benzene was poured dropwise into a solution of 3.6 g chloroacetyl chloride in 4 ml benzene with cooling and stirring. The bottom layer of oil was washed with benzene and ether and allowed to stand in a vacuum desiccator. After 4 hours the oil had solidified. Yield of crude, washed product 3.3 g or 70% of theory. The salt was purified by crystallization from a mixture of alcohol and ether. White needles, m.p. 169-172° with decomposition.

Found %: Cl 28.33, 28.37. $C_{10}H_{11}NSCl_2$. Calculated %: Cl 28.62.

Synthesis of Dyes

1. 3-Methyl-2-trinitrophenyl-methylenebenzothiazoline

This preparation was synthesized by four methods for comparison.

a) 0.9 g of 2-methylbenzothiazole methylmethosulfate was dissolved in 10 ml water and mixed in a separating funnel with 15 ml benzene and 0.6 g solid NaOH. The mixture was agitated, the benzene solution of the methine base was separated and dried for a short time with anhydrous Na_2SO_4, and then a solution of 0.4 g picryl chloride in 10 ml benzene was added to it The mixture was heated for an hour on the water bath. The quaternary salt was filtered off and the benzene solution was concentrated. The dye that separated on cooling was crystallized from benzene with addition of ether. Greenish prisms melting at 202-203° with decomposition.* λ_{max} in benzene 552 mμ. Yield 0.25 g or 42% of the theoretical.** $E \cdot 10^{-4}$ 3.

Found*** %: N 14.83, 14.78. $C_{15}H_{10}O_6N_4S$. Calculated %: N 14.97.

b) 0.25 g 2-methylbenzothiazole methylmethosulfate and 0.22 g picryl chloride were dissolved in 5 ml absolute alcohol by heating. Into the mixture was stirred a solution of 0.2 g triethylamine in 2 ml alcohol. The mixture was allowed to stand for 10 minutes and then cooled. The dye was filtered, washed repeatedly with water, alcohol and ether and dried in a vacuum-desiccator. M.p. 201-202° with decomposition. A mixed sample with the preparation obtained by method a) did not give a m.p. depression. Yield 0.3 g or 88% of theory.

c) 0.25 g 2-methylbenzothiazole methylmethosulfate, 0.24 g methylpicryl sulfide [7] and 0.2 g triethylamine were mixed and treated as in method b). During the reaction the mercaptan separated. Yield of washed product 0.28 g or 82.3% of theory. M.p. 200-201° with decomposition. No depression in mixed m.p. test with the preparation obtained by method a).

d) 0.5 g 2-methylbenzothiazole methylmethosulfate, 0.23 g trinitroanisole and 0.2 g triethylamine were mixed and treated as for method b). The yield of washed product was 0.27 g or 79.4% of theory. M.p. 199-200° with decomposition. A mixture with the preparation obtained by method a) did not show a m.p. depression.

2. 3-Methyl-6-nitro-2-trinitrophenyl-methylenebenzothiazoline

0.5 g 3-methyl-6-nitro-2-methylenebenzothiazoline [1] was dissolved in 20 ml nitrobenzene and a solution of 0.3 g picryl chloride in 10 ml nitrobenzene was added. The mixture was heated for 1½ hours on the water bath. The quaternary salt was filtered off, and from the nitrobenzene solution a dye was crystallized in the form of greenish-black prisms with a metallic luster. After washing with water, alcohol and ether the m.p. was 215° with decomposition. λ_{max} in benzene 533 mμ. Yield 0.32 g or 64% of the theoretical.

Found %: N 16.63. $C_{15}H_9O_8N_5S$. Calculated %: N 16.70.

3. 3-Methyl-2-trinitrophenylmethylene-α-naphthothiazoline

A solution of 0.7 g 3-methyl-2-methylene-α-naphthothiazoline [1] in 20 ml benzene was mixed with a solution of 0.4 g picryl chloride in 10 ml benzene and heated for an hour on the water bath. The product after evaporation of the benzene solution was crystallized from toluene. Black crystals. Yield 0.38 g or 56% of theory. λ_{max} in benzene 569 mμ. M.p. 207-208° with decomposition.

Found %: N 13.29. $C_{19}H_{12}O_6N_4S$. Calculated %: N 13.52.

4. 3-Methyl-2-(2',4'-dinitrophenyl)-methylenebenzothiazoline

A solution of 3-methyl-2-methylenebenzothiazoline (prepared from 1.1 g 2-methylbenzothiazole methylmethosulfate) in 15 ml benzene and 0.4 g 2,4-dinitrochlorobenzene in 8 ml benzene was boiled on the water bath for 3 hours. The quaternary salt was filtered off and the benzene solution was concentrated. The dye that came down on cooling was crystallized from benzene. Black needles with m.p. 243-244° with decomposition λ_{max} 502 mμ. Yield 0.19 g or 29% of the theoretical.

Found %: N 12.50. $C_{15}H_{11}O_4N_3S$. Calculated %: N 12.76.

5. 3-Methyl-2-(2',6'-dinitro-4'-trifluoromethylphenyl)-methylenebenzothiazoline

A solution of 3-methyl-2-methylenebenzothiazoline (prepared from 1.1 g 2-methylbenzothiazole methylmethosulfate) in 15 ml benzene and 0.54 g 3,5-dinitro-4-chlorobenzotrifluoride in 8 ml benzene were boiled on the water bath for 2½ hours. The dye that separated after evaporation of the benzene solution was crystallized from a mixture of benzene and ether. Black needles, m.p. 195-196°; λ_{max} 510 mμ. Yield 0.27 g or 35% of the theoretical.

Found %: N 10.33. $C_{16}H_{10}O_4N_3SF_3$. Calculated %: N 10.56.

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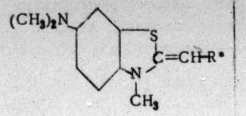
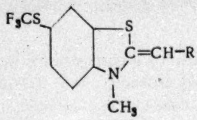
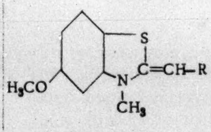
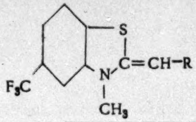
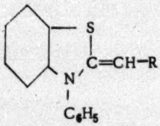
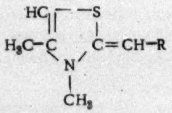
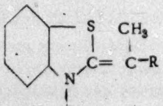
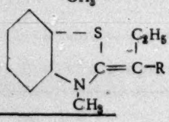
* All the dyes described in this paper are readily soluble in benzene, less soluble in chloroform and dichloroethane, poorly soluble in ether and almost insoluble in alcohol.

** The yields of dyes are calculated on the picryl chloride.

*** Before analysis all the preparations were dried in vacuum for 2 hours at 80°.

TABLE 3

Prep. No.	Formula of dye	Amount of quaternary salt (in g)	Aromatic nitro compound (g)	Method of prep.	Condensation
					Amt. of abs. alcohol (ml)
1	2	3	4	5	6
7		Amount of quaternary salt (in g) 0.28	Methyl-picryl sulfide 0.22	1-c	10
8		2-Methyl-6-trifluoro-methylmercaptobenzo-thiazole methoiodide 0.13	Picryl chloride 0.08	1-b	5
9		2-Methyl-5-methoxy-benzothiazole methyl-methosulfate 0.15	Picryl chloride 0.12	1-b	5
10		2-Methyl-5-trifluoro-methylbenzothiazole methoiodide 0.2	Methyl-picryl sulfide 0.15	1-c	5
11		2-Methylbenzothiazole phenoiodide 0.25	Methyl-picryl sulfide 0.18	1-c	12
12		2,4-Dimethylthiazole methylmethosulfate 0.48	Picryl chloride 0.5	1-b	15
13		2-Ethylbenzothiazole methylmethosulfate 0.86	Picryl chloride 0.74	1-b	20
14		2-Propylbenzothiazole 0.37	Picryl chloride 0.3	1-b	10

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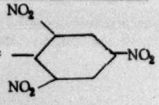
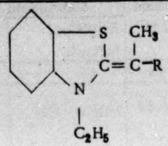
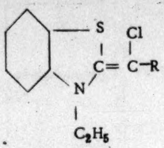
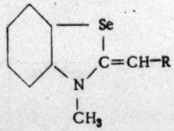
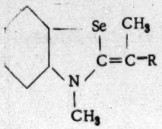
* R = 

conditions		Solvent for crystallization	Yield (%)	Appearance	$\lambda_{max.}$ (mμ) in benzene	M.p. with decomp.	Analysis		
$N(C_2H_5)_3$ (g)	Duration of heating (min)						Found % N	Calculated	
								Empirical formula	% N
7	8	9	10	11	12	13	14	15	16
0.2	5	Mixture of benzene and ether	81	Black crystals	599	206-207	16.85	$C_{17}H_{15}O_6N_5S$	16.78
0.07	2	Alcohol	78	Bronze crystals	550	201-202	11.56	$C_{16}H_9O_6N_4S_2F_3$	11.81
0.1	2	Benzene	81	Green crystals	560	201-202	13.79	$C_{16}H_{12}O_7N_4S$	13.86
0.15	5	Mixture of benzene and ether	83	Bronze needles	535	209-210	12.81	$C_{16}H_9O_6N_4SF_3$	12.67
0.2	5	Benzene	79	Black crystals	554	204-205	12.64 12.62	$C_{20}H_{12}O_6N_4S$	12.84
0.4	3	Benzene	82	Green crystals	550	189-190	16.57	$C_{12}H_{10}O_6N_4S$	16.76
0.6	2	Benzene	83	Violet crystals	605	155-156	14.36 14.28	$C_{16}H_{12}O_6N_4S$	14.43
0.25	2	Benzene	86	Violet crystals	605	153-154	13.75	$C_{17}H_{14}O_6N_4S$	13.93

TABLE 3 (Continued)

1	2	3	4	5	6
15		2-Ethylbenzothiazole ethoiodide 0.32	Picryl chloride 0.25	1-b	15
16		2-Chloromethylbenzothiazole ethochloride 0.3	Picryl chloride 0.3	1-b	10
17		2-Methylbenzoselenoazole methylmethosulfate* 0.24	Picryl chloride 0.25	1-b	10
18		2-Ethylbenzoselenazole methylmethosulfate*	Picryl chloride 0.22	1-b	10

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* The authors thank F. S. Babichev for putting the quaternary salts of benzoselenazole at their disposal.

6. 3-Ethyl-2-trinitrophenylbenzothiazoloneimine

A solution of 0.6 g 3-ethylbenzothiazoloneimine in 15 ml benzene and 0.42 g picryl chloride in 8 ml benzene was boiled on the water bath for an hour. The precipitated 2-aminobenzothiazole ethochloride was filtered off, and the benzene solution was concentrated. The dye that came down on cooling was crystallized from benzene. Stout yellow crystals with m.p. 194°; λ_{max} 430 mμ. Yield 0.4 g or 61.5% of the theoretical.

Found %: N 17.86, 17.77. $C_{15}H_{11}O_6N_5S$. Calculated %: N 17.99.

All the remaining dyes were prepared not from the methine bases but directly from the quaternary bases as for preparation 1 by methods b) or c).

The conditions of their preparation and their properties are presented in Table 3. All the compounds were analyzed for nitrogen with exception of preparation 16, in which the chlorine was determined.

SUMMARY

1. 18 dyes were synthesized by condensation of the methine bases and quaternary salts of heterocyclic bases with aromatic nitrochloro compounds.

2. It is shown that methylpicryl sulfide and trinitroanisole enter into the condensation reaction with quaternary salts of heterocyclic bases.

7	8	9	10	11	12	13	14	15	16
0.2	2	Benzene	82	Violet needles	610	151-152	13.72 13.75	$C_{17}H_{14}O_6N_4S$	13.93
0.24	2	Mixture of benzene and ether	60	Black crystals	605	145-147	8.15 8.28 (Cl)	$C_{16}H_{11}O_6N_4SCl$	8.42 (Cl)
0.2	2	Washed with hot alcohol; crystallization from benzene	45	Black crystals	560	202-203	13.01	$C_{15}H_{10}O_6N_4Se$	13.29
0.2	2	Washed with hot alcohol; crystallization from benzene	39	Black crystals	605	155-156	12.58	$C_{16}H_{12}O_6N_4Se$	12.87

3. Introduction into the benzene ring of benzothiazole of electropositive substituents causes a shift of the absorption maximum of the dye in the long-wave direction; introduction of electronegative substituents shifts the absorption maximum toward shorter wave lengths.

4. Replacement of the hydrogen in the methylene group of a dye by CH_3, C_2H_5 and Cl leads to a marked deepening of color. This color change is evidently due to steric hindrance which renders the molecule of the dye noncoplanar.

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* See Consultants Bureau translation, p. 149.

** See Consultants Bureau translation, p. 1971.

*** See Consultants Bureau translation, p. 139.

**** See Consultants Bureau translation, p. 543.

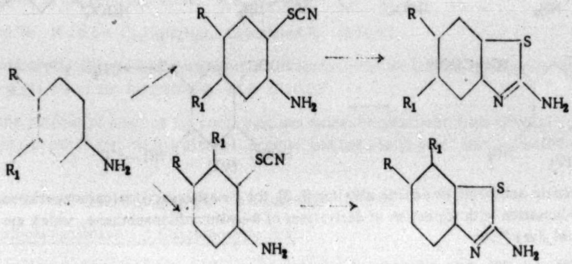
BENZOTHIAZOLE DERIVATIVES

IV. SYNTHESIS OF DERIVATIVES OF 2-AMINOBENZOTHIAZOLE-5,6- AND -6,7-DICARBOXYLIC ACIDS

I. A. Solovyeva and G. I. Arbuzov*

In the thiocyanation of amines of the benzene series containing various substituents in the para-position, the thiocyanogen group easily enters the para-position to the amino group. In the majority of cases the so-formed o-aminothiocyanobenzenes have poor stability and readily isomerize to derivatives of 2-aminobenzothiazole. This process goes especially rapidly in an acid medium at elevated temperature [1,2,3,4].

It was a matter of interest to study the processes of thiocyanation and ring-closure of the obtained o-thiocyanoamino compounds into derivatives of 2-aminobenzothiazoles in the case of 3,4-disubstituted anilines.



In this case formation could be expected of two isomeric thiocyano derivatives which would then give the corresponding two 2-aminobenzothiazoles.

We studied this reaction with reference to the dimethyl ester of 4-aminophthalic acid (R, R_1 = $COOCH_3$), thiocyanation being effected by adding bromine to the acetic acid solution of the amine in presence of 2.4 moles of potassium thiocyanate at −3 to −4° [1].

In this way we obtained two isomeric dicarbomethoxy-2-aminobenzothiazoles with melting points of 233-234° and 180-181° (in yields of 38 and 21.5% of the theoretical, respectively). Separation of the isomers was readily effected by taking advantage of the considerably lower solubility in ethyl alcohol of the dicarbomethoxy-2-aminobenzothiazole with m.p. 233-234°.

Consequently in the thiocyanation of the dimethyl ester of 4-aminophthalic acid, the SCN group enters at both of the ortho positions to the amino group.

Saponification of the isomeric dicarbomethoxy-2-aminobenzothiazoles (I and II) readily gave the free 2-aminobenzothiazole dicarboxylic acids. These compounds do not have a definite melting point and are very sparingly soluble in organic solvents (slightly more soluble in pyridine).

For the determination of their structure, the compounds were heated with concentrated KOH solution at 110-150° until ammonia ceased to come off, and the resultant aminomercaptophthalic acids were converted, by reaction with a salt of chloroacetic acid, into the corresponding 2-aminodicarboxyphenylmercaptoacetic acids which we isolated in the form of the acid potassium salts. In an acid medium, like other similar compounds [5,6,7], these salts are extremely unstable and readily lose water to give the corresponding lactams [derivatives of 3-hydroxy-1,4-benzothiazine (V), (VI)].

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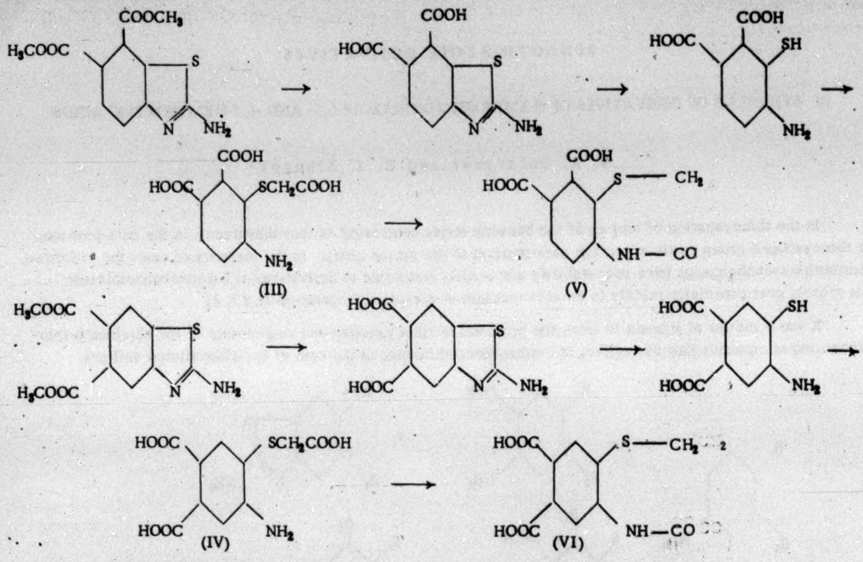
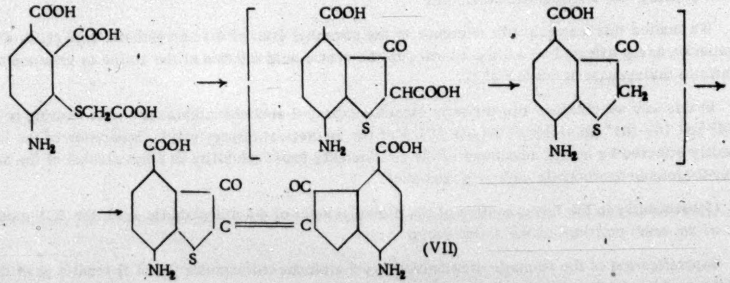


When heated with acetic anhydride or caustic alkalies [8,9], the o-carboxyarylmercaptoacetic acids readily undergo intramolecular condensation with formation of derivatives of 3-hydroxythionaphthene, which are converted by oxidation into thioindigoid dyes [7,9].

Out of the 2-aminodicarboxyphenylmercaptoacetic acids prepared by us, only the 5,6-dicarboxy derivative (III) could form a 3-hydroxythionaphthene derivative by this reaction, and therefrom the thioindigoid dye (VII):



The prepared aminodicarboxyphenylmercaptoacetic acids were heated with acetic anhydride in presence of sodium acetate; the reaction mixture was made alkaline and to the filtered solution was added a solution of potassium ferricyanide.

In the case of the substituted mercaptoacetic acid synthesized from the dimethyl ester of 2-aminobenzothiazole dicarboxylic acid with m.p. 180-181°, heating with acetic anhydride resulted in evolution of carbon dioxide, while during oxidation of the obtained solution the color changed from yellow-brown to deep blue-red. Acidification of this solution brought down a precipitate of a dye whose composition corresponded to 4,4'-dicarboxy-7,7'-diaminothioindigo.

When the isomeric 2-aminodicarboxyphenylmercaptoacetic acid, prepared from the dimethyl ester with m.p. 233-234°, was treated similarly, no carbon dioxide came off; nor was formation of a dye observed when potassium ferricyanide was added to the alkaline solution of the reaction product.

In the light of these data we may claim to have established that 2-aminodicarbomethoxybenzothiazole with m.p. 180-181° is the 6,7-dicarbomethoxy derivative (I). Accordingly the product melting at 233-234° will have structure (II).

EXPERIMENTAL

(in collaboration with A. G. Guseva)

Dimethyl Esters of 2-Aminobenzothiazole-5,6dicarboxylic acid and of 2-aminobenzothiazole-6,7dicarboxylic acid

A mixture of 10.45 g dimethyl ester of 4-aminopthalic acid (0.05 mole) and 12 g potassium thiocyanate (0.12 mole) was dissolved in 75 ml 95% acetic acid, and into the resultant solution was stirred at −3 to −4° a solution of 10 g bromine (0.06 mole) in 15 ml 95% acetic acid over a period of 20 minutes. The reaction mass was stirred for 2 hours and left overnight. The liquid was then diluted with 200 ml water, filtered from the small precipitate and neutralized with aqueous ammonia. The light-yellow precipitate was filtered, washed with water and dried. Weight 9.95 g (75% of the theoretical). M.p. 180-210°. The precipitate was crystallized from 200 ml ethyl alcohol. Yield 5.0 g (38% of the theoretical). M.p. 228-230°.

For the purpose of analysis the product was twice recrystallized from ethyl alcohol. Colorless needles, readily soluble in acetone, ethyl alcohol (boiling) and acetic acid; sparingly soluble in cold ethyl alcohol, very sparingly soluble in benzene and ether. M.p. 233-234°.

Found %: N 10.59. $C_{11}H_{10}O_4N_2S$. Calculated %: N 10.53.

The alcoholic filtrate was evaporated to a volume of 10 ml and the precipitate was filtered and dried. Weight 2.85 g (21.5% of the theoretical). M.p. 170-172°.

For the purpose of analysis the compound was twice recrystallized from ethyl alcohol. Yellowish plates. Readily soluble in ethyl and methyl alcohol, acetone and hot acetic acid; almost insoluble in ether and benzene. M.p. 180-181°.

Found %: N 10.41. $C_{11}H_{10}O_4N_2S$. Calculated %: N 10.53.

2-Aminobenzothiazole-5,6-dicarboxylic acid

2.66 g dimethyl ester of 2-aminobenzothiazole-5,6-dicarboxylic acid with m.p. 233-234° (0.01 mole) and a solution of 3.4 g KOH (0.06 mole) in 170 ml water were refluxed for 2½ hours. The alkaline solution was filtered and acidified with hydrochloric acid until the reaction to Congo was sharply acid. After 30 minutes the colorless precipitate was filtered off, mixed with 100 ml hot water, again filtered, washed on the filter with hot water and dried. Yield 2.14 g (90% of the theoretical). Colorless crystalline powder. Almost insoluble in common organic solvents, fairly readily soluble in pyridine, readily soluble in sodium carbonate solution. M.p. above 300°.

For the purpose of analysis the compound was purified by boiling with alcohol and by two reprecipitations from sodium carbonate solution.

Found %: N 11.88, equivalent 120.20. $C_9H_6O_4N_2S$. Calculated %: N 11.76; equivalent 119.07.

2-Aminobenzothiazole-6,7-dicarboxylic acid

To 2.66 g dimethyl ester of 2-aminobenzothiazole-6,7-dicarboxylic acid with m.p. 180-181° (0.01 mole) was added a solution of 3.13 g KOH (0.056 mole) in 150 ml water, and the mixture refluxed for 1½ hours. The alkaline solution was filtered from the small precipitate and acidified with hydrochloric acid until the reaction to Congo was sharply acid. After 30 minutes the colorless precipitate was filtered, stirred with 100 ml hot water, again filtered, washed with hot water on the filter and dried. Yield 2.19 g (92% of the theoretical).

Colorless crystalline powder. Almost insoluble in the usual solvents, rather more soluble in pyridine, readily soluble in sodium carbonate solution. M.p. above 300°.

For the purpose of analysis the substance was purified by digestion with alcohol and by two reprecipitations from sodium carbonate solutions.

Found %: N 11.53; equivalent 119.70. $C_9H_6O_4N_2S$. Calculated %: N 11.76; equivalent 119.07.

Lactam of 2-amino-5,6-dicarboxyphenylmercaptoacetic acid

1.33 g dimethyl ester of 2-aminobenzothiazole-6,7-dicarboxylic acid with m.p. 180-181° was mixed with a solution of 2.8 g KOH in 2.5 ml water, and the mixture refluxed for 3 hours on an oil bath with gradual rise of temperature from 110° to 130° (oil temperature); after that, heating was continued in the open flask at 150-155° until ammonia ceased to come off (30-40 minutes). To the cooled mixture was added a solution of 0.47 g chloroacetic acid and 0.28 g KOH in 3 ml water, and the mixture heated for 30 minutes on the water bath at 65-75°. To the cooled solution was added 6.5 ml glacial acetic acid and the resultant syrupy mass was diluted with 50 ml alcohol. The alcohol was decanted off, the precipitate of the acid potassium salt of 2-amino-5,6-dicarboxyphenylmercaptoacetic acid was washed with absolute alcohol until completely crystallized, rapidly filtered, and dried in a vacuum desiccator. Weight 1.1 g. The product was very hygroscopic and without further purification was used for the preparation of the thioindigoid dye.

When the alkaline solution of 2-amino-5,6-dicarboxyphenylmercaptoacetic acid was acidified with hydrochloric acid, the acid solution deposited on standing a precipitate of the lactam; this was filtered, washed with water and recrystallized from hot water. Fine yellow needles; soluble in hot water, insoluble in alcohol, ether, benzene and acetic acid. Sinters at above 30[illegible]

Found %: N 5.36; equivalent 125.8. $C_{10}H_{17}O_5NS$. Calculated %: N 5.53; equivalent 126.6.

4,4'-Dicarboxy-7,7'-diaminothioindigo

To 1.1 g of the acid potassium salt of 2-amino-5,6-dicarboxyphenylmercaptoacetic acid was added 3.2 ml acetic anhydride and 0.66 g calcined sodium acetate, and the mixture was boiled for 45 minutes. Carbon dioxide came off during the treatment. To the cooled reaction mass was then added 12 ml 20% NaOH solution; the solution was boiled for 20 minutes, cooled and filtered. To the yellow-brown filtrate was added a solution of 5.26 g potassium ferricyanide in 20 ml water, the color of the solution changing to blue-red. The mixture was shaken for a few minutes and acidified with hydrochloric acid until acid to Congo. The red-brown precipitate of the dye was filtered, washed with water and alcohol and dried.

For the purpose of purification the dye was reprecipitated from sodium carbonate solution with hydrochloric acid, filtered, washed, dried and recrystallized from ethyl alcohol. Light-brown crystals, m.p. 210-212°. Fairly good solubility in methyl and ethyl alcohol and acetic acid; less good in acetone. Insoluble in ether and benzene; readily soluble in sodium carbonate solution.

Found %: N 6.98. $C_{18}H_{10}O_6N_2S_2$. Calculated %: N 6.76.

Lactam of 2-amino-4,5-dicarboxyphenylmercaptoacetic acid

To 1.33 g dimethyl ester of 2-aminobenzothiazole-5,6-dicarboxylic acid with m.p. 233-234° was added a solution of 2.8 g KOH in 2.5 ml water; the mixture was refluxed in a flask on an oil bath at 120-130° (oil temperature) for 4 hours and then heated in the open flask at 140-150° until ammonia ceased to come off (45-60 minutes). To the cooled mixture was added a solution of 0.47 g chloroacetic acid and 0.28 g KOH in 3 ml water, and the mixture was heated for 30 minutes on the water bath at 65-70°. To the cooled solution was added dropwise 2.5-3 ml glacial acetic acid when a precipitate was formed, and the viscous mass was carefully stirred with 50 ml alcohol. The precipitate of the acid potassium salt of 2-amino-4,5-dicarboxyphenylmercaptoacetic acid was filtered off, washed a few times with alcohol and dried at 80°. Weight 1.22 g. Readily soluble in water, very sparingly in ethyl alcohol.

When the 2-aminocarboxyphenylmercaptoacetic acid was heated with acetic anhydride in presence of sodium acetate, no carbon dioxide was evolved. When the reaction mass was made alkaline and treated with potassium ferricyanide, formation of a dye was not observed. On acidification with hydrochloric acid of the alkaline solution of 2-aminodicarboxyphenylmercaptoacetic acid, gradual separation (quicker if heated) occurred of a colorless precipitate of the lactam of 2-amino-4,5-dicarboxyphenylmercaptoacetic acid. This was filtered off, washed with water and recrystallized from hot water. Fine colorless crystals. Readily soluble in hot water, insoluble in alcohol, benzene, ether and acetic acid. Sinters at a temperature above 300°.

Found %: N 5.32; equivalent 127.2. $C_{10}H_{17}O_5NS$. Calculated %: N 5.53; equivalent 126.6.

SUMMARY

1. The thiocyanation of the dimethyl ester of 4-aminophthalic acid was studied in a medium of acetic acid. It was shown that a mixture is formed of the esters of 2-aminobenzothiazole-5,6- and -6,7-dicarboxylic acids.

2. The lactams of 4,5- and 5,6-dicarboxy-2-aminophenylmercaptoacetic acids were prepared.

3. 4,4'-Dicarboxy-7,7'-diaminothioindigo was synthesized from the ester of 2-aminobenzothiazole-6,7-dicarboxylic acid.

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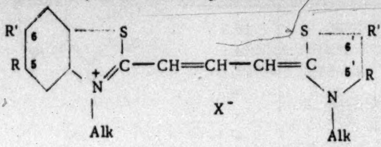
All-Union Cinephoto Research Institute

COPLANARITY OF THE DIMETHYLAMINO GROUP WITH THE BENZENE RING AND ITS AUXOCHROMIC ACTION. I.

A. I. Kiprianov and I. N. Zhmurova

The influence of the dimethylamino group on the color of a dye is associated with transfer of the free electron pair of the nitrogen atom to the benzene ring and subsequently to a conjugated chain [1]. A necessary condition for such an electron transfer is the location of the dimethylamino group in the same plane as the benzene ring. If a voluminous substituent is introduced into the ortho-position to the dimethylamino group, the latter moves out of the plane of the ring and its influence on the color is partly or completely eliminated. The weakening of the auxochromic action of the dimethylamino group due to introduction of a substituent in the ortho-position has been described by I. I. Levkoev with reference to cyanine dyes [2] and by Remington with reference to dialkylanilines [3]. The observations of I. I. Levkoev related mainly to substituents of a polar character for which it is difficult to segregate the steric effect from the electronic effects. We have investigated this phenomenon in cyanine dyes containing bulky alkyl radicals in the ortho-position to the amino groups. To a first approximation the electronic effect of such radicals may be neglected. With this objective we synthesized a series of new tetrasubstituted thiacarbocyanines with the general formula:



where R = NH_2, $NHCOCH_3$ or $N(CH_3)_2$, R' = CH_3 or $C(CH_3)_3$, Alk = CH_3 or C_2H_5 , X = anion of the dye.

The absorption maxima and the molecular extinctions of these dyes are enumerated in Table 1. For comparison the table includes data for some previously known dyes (1,2,4,7,10).

TABLE 1

No.	R	R'	Alk	λ_{max} in mμ	$\epsilon_{max} \cdot 10^{-4}$
1	H	H	CH_3	558	16.5
2	H	CH_3	C_2H_5	563	14.5
3	H	$C(CH_3)_3$	CH_3	563	14.9
4	$NHCOCH_3$	H	C_2H_5	577	–
5	$NHCOCH_3$	CH_3	C_2H_5	575	–
6	$NHCOCH_3$	$C(CH_3)_3$	CH_3	568	–
7	NH_2	H	C_2H_5	596	–
8	NH_2	CH_3	C_2H_5	594	–
9	NH_2	$C(CH_3)_3$	CH_3	592	–
10	$N(CH_3)_2$	H	C_2H_5	608	8.2
11	$N(CH_3)_2$	CH_3	C_2H_5	575	10.1
12	$N(CH_3)_2$	$C(CH_3)_3$	CH_3	570	14.1

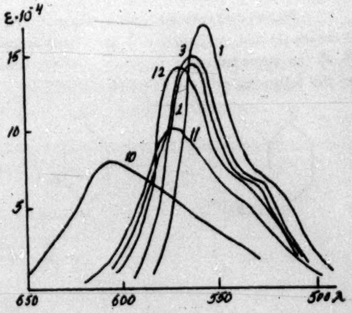


Fig. 1.

The absorption curves of preparations 1,2,3,10,11 and 12 are shown in Fig. 1.

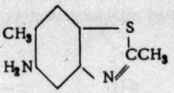
In themselves the alkyl groups R' exhibit little influence on the absorption (preparations 1,2,3). Substitution of the hydrogen atoms in the 5,5'-position by dimethylamino groups sharply shifts the absorption curve. The absorption maximum is displaced into the long-wave part of the spectrum to the extent of 50 mμ, the absorption band is broadened, and its intensity lowered (10). The red-violet color of the alcoholic solution of the dye changes to dark-blue. If, however, methyl radicals are introduced in the 6,6'-position, i.e. in the ortho-position to the dimethylamino groups, then the influence of the dimethylamino groups is partly paralyzed as it were. The absorption maximum of the corresponding preparation (11) differs from that of the unsubstituted thiacarbocyanine by only 12 mμ, the absorption intensity increases, and in alcoholic solution the dye acquires a violet color. Replacement of the two methyl groups by two tertiary butyl groups causes the absorption curve to approach still more closely the curve of the unsubstituted thiacarbocyanine. In this case the difference in the positions of the absorption maxima is 7 mμ, and if we compare such a tetrasubstituted dye (12) with the disubstituted dye containing the same tertiary butyl groups but not containing dimethylamino groups (3), then we find that their absorption curves are almost identical. It is impossible to distinguish between these two dyes by the color of their alcoholic solutions. Alkyl radicals in ortho-positions are substantially without influence on the auxochromic action of acetylamino and unsubstituted amino groups (preparations 4,5,6 and 7,8,9). A brief exposition of this part of our investigation has already been published [4].

Compounds that we prepared later are listed in Table 2 and represent isomers of the dyes in Table 1; they differ from the latter in the distribution of the alkyl and amino groups. As we see from Table 2 and Fig. 2, in these preparations also the alkyl group adjacent to the dimethylamino group partly suppresses the auxochromic effect of the latter. In this table are also listed the known dyes 13, 15, 18 and 21 for comparison.

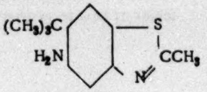
Preparation of the above-described tetrasubstituted thiacarbocyanines necessitated as intermediates the benzothiazole derivatives (I) and (II) as well as their isomers (III) and (IV).

TABLE 2

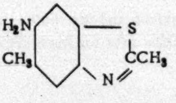
No.	R	R'	Alk	λ_{max} in mμ	$\epsilon_{max}\cdot10^{-4}$
1	H	H	CH_3	558	16.5
13	CH_3	H	C_2H_5	563	14.5
14	$C(CH_3)_3$	H	CH_3	565	14.4
15	H	$NHCOCH_3$	C_2H_5	579	–
16	CH_3	$NHCOCH_3$	CH_3	575	–
17	$C(CH_3)_3$	$NHCOCH_3$	CH_3	570	–
18	H	NH_2	C_2H_5	596	–
19	CH_3	NH_2	CH_3	594	–
20	$C(CH_3)_3$	NH_2	CH_3	592	–
21	H	$N(CH_3)_2$	C_2H_5	612*	11.7
22	CH_3	$N(CH_3)_2$	CH_3	575	12.4
23	$C(CH_3)_3$	$N(CH_3)_2$	CH_3	570	14.3



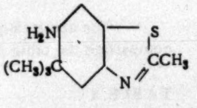
(I)



(II)

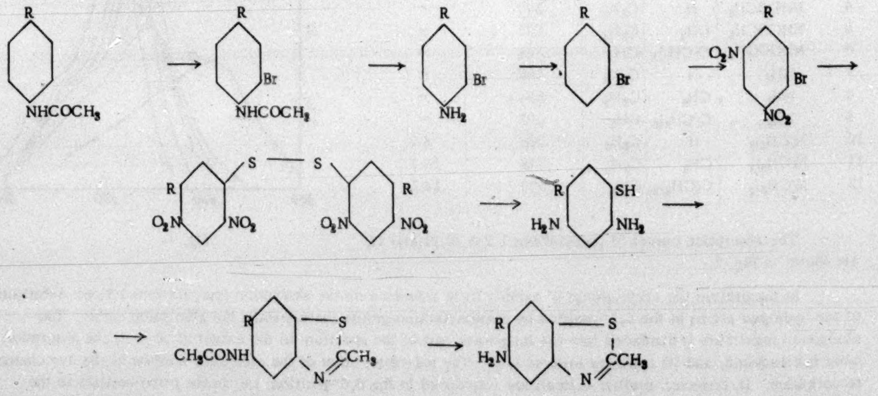


(III)

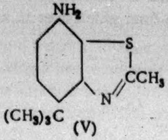


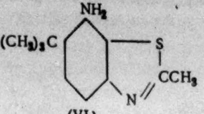
(IV)

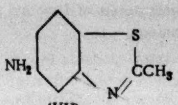
Of these four bases, only 2,6-dimethyl-5-aminobenzothiazole (I) and its isomer (III) have been described in patents [5,9]; the other two were unknown. We prepared (I) and (II) by the following scheme [R = CH_3, $C(CH_3)_3$]:



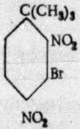
There can be no doubt about the structure of preparation (I) since 3-bromo-4,6-dinitrotoluene, the intermediate in its synthesis, has been described in the literature [6]. Concerning base (II), it was necessary to demonstrate that the structure was that stated and not that of one of its isomers (V, VI, VII):

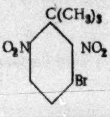

(V)


(VI)


(VII)

which could be obtained if dinitro products with the structures (VIII) and (IX) were formed in the nitration of m-bromo-tert. butylbenzene:


(VIII)


(IX)

The following facts support the assumption that we actually obtained base (II).

1. Formation of nitro products (VIII) and (IX) during nitration of m-bromo-tert. butylbenzene is highly improbable due to steric hindrance.

2. When the quaternary salts of benzothiazole (V) and (VI) are condensed with ethyl orthoformate, they must give thiacarbocyanines whose color differs but slightly from that of the thiacarbocyanine not containing amino groups. E. D. Sych showed that in 7,7'-positions, amino groups have little influence on the color of thiacarbocyanines [7]. Moreover, our base gave a deeply colored thiacarbocyanine with an absorption maximum at 592 mμ.

3. Structures (V) and (VII) must be excluded because deamination of our base yielded 2-methyl-6-tert. butylbenzothiazole. This was proved by the absence of depression in melting point determinations of mixed specimens of picrates of our base and of 2-methyl-6-tert. butylbenzothiazole.

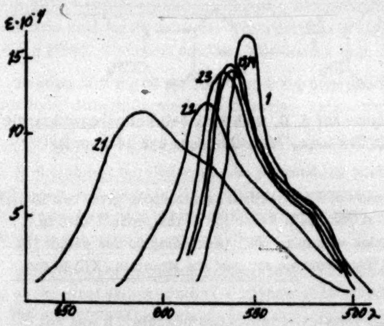
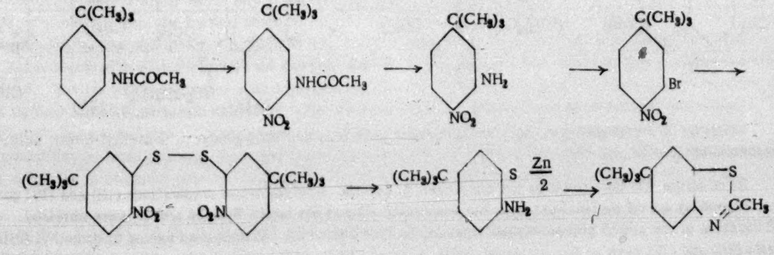


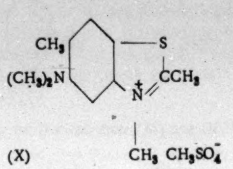
Fig. 2.

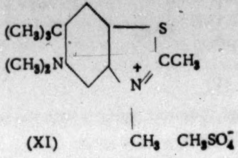
We synthesized 2-methyl-6-tert. butylbenzothiazole by the following scheme:



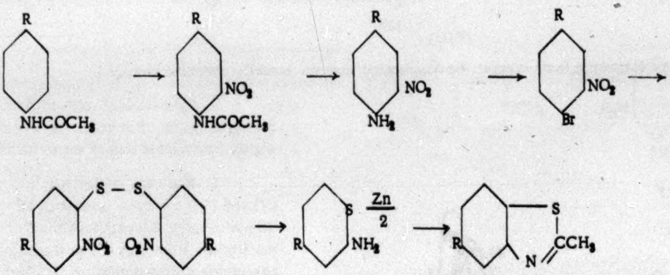
The dye 3 was prepared from the quaternary salt of 2-methyl-6-tert. butylbenzothiazole.

The acetyl derivatives of bases (I) and (II) were likewise converted into the quaternary salts and then into dyes 5 and 6. Saponification of the acetyl groups of the dyes gave dyes 8 and 9. Treatment of bases (I) and (II) with excess of dimethyl sulfate gave us the quaternary salts (X) and (XI) from which dyes 11 and 12 were prepared.


(X)


(XI)

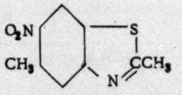
The isomeric bases (III) and (IV) were prepared through 2-methyl-5-alkylbenzothiazoles by the following route [R = CH_3 or $C(CH_3)_3$]:

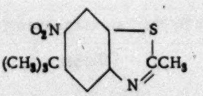


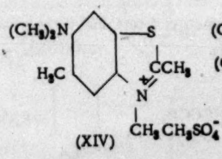
This synthetic scheme was worked out by A. I. Kiprianov and E. D. Sych for 2,5-dimethylbenzothiazole [8]. We prepared 2-methyl-5-tert. butylbenzothiazole for the first time. We synthesized dye 14 from its quaternary salt.

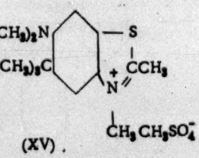
2-Methyl-5-alkylbenzothiazoles were nitrated. Nitration of 2,5-dimethylbenzothiazole gives two isomeric nitro products, one of which melts at 152-154° and the other at 133-134°. Reduction of the product with m.p. 152-154° with tin chloride and hydrochloric acid gave an amine with m.p. 168°. According to one patent [9], this is the m.p. of 2,5-dimethyl-6-aminobenzothiazole. For this reason we assigned the structure (XII) to the nitro product with m.p. 152-154°.

The second isomer with m.p. 133-134° is evidently 2,5-dimethyl-4-nitrobenzo thiazole. It was not further investigated.


(XII)


(XIII)


(XIV)


(XV).

Nitration of 2-methyl-5-tert. butylbenzothiazole gave only one nitro product: 2-methyl-5-tert. butyl-6-nitrobenzothiazole (XIII).

Its structure was confirmed by the deep color of dye 20. Acetylation of preparations (III) and (IV) gave the corresponding acetyl derivatives; from the quaternary salts of the latter, dyes 16 and 17 were obtained. Saponification of the acetyl groups in these dyes led to dyes 19 and 20. Action of an excess of dimethyl sulfate on bases (III) and (IV) gave us the quaternary salts (XIV) and (XV), from which the dyes 21 and 22 were obtained.

Apart from 3 and 14, all the dyes that we synthesized in the first and second series are amorphous powders which could only be purified by chromatography. Their yields did not exceed 23%. Owing to the difficulty of purification, dyes 8, 9, 16, 19 and 20 were not isolated in the pure state.

EXPERIMENTAL

2,6-Dimethyl-5-acetylaminobenzothiazole and 2,6-dimethyl-5-aminobenzothiazole (I). To a warm solution of 26 g 3-bromo-4,6-dinitrotoluene (prepared by nitration of m-bromotoluene [6]) in 250 ml alcohol was gradually added with shaking a hot mixture of 18 g crystalline sodium sulfide, 2.4 g sulfur and 10 ml alcohol. After all had been added, the mixture was boiled for 3 hours. The yellow precipitate of 2,2',4,4'-tetranitro-5,5'-dimethyldiphenyldiphenyldisulfide was filtered and washed with water. Yield 18 g (82%) *. 18 g disulfide, 90 g tin and 150 ml concentrated HCl were gently refluxed until all the tin had dissolved and then boiling was continued for an hour. The whole of the disulfide dissolved. The solution was diluted with water and the tin was precipitated by heating with hydrogen sulfide. The precipitate was filtered, the solution was evaporated to dryness in vacuum. To the dry residue was added 30 ml acetic anhydride and 100 ml glacial acetic acid. The mixture was boiled for 3 hours, then diluted with water and neutralized with ammonia. The residue (2,6-dimethyl-5-acetylaminobenzothiazole and residual tin) was dried and extracted with benzene in a Soxhlet apparatus. Yield 7 g (31%). Recrystallization from benzene gave fine, slightly yellow needles, m.p. 176-178° **; according to patent data [5] the m.p. is 178°.

Methiodide: light-yellow prisms (from alcohol), m.p. 216-218° with decomposition.

Found %: I 35.16, 35.18. $C_{12}H_{15}ON_2SI$. Calculated %: I 35.08.

Precipitation of tin by hydrogen sulfide after reduction of the disulfide is not obligatory. The solution may be evaporated to dryness on the water bath after completion of the reduction, and the dry residue (a mixture of tin salts and the hydrochloride of 2,4-diamino-5-methylthiophenol) may be worked up as described above. By this method the yield is not reduced.

2,5-Dimethyl-6-aminobenzothiazole was prepared by heating 1.5 g of the preceding product with 10 ml dilute sulfuric acid for 30 minutes. The solution was digested with carbon, filtered and neutralized with ammonia. Yield 0.9 g (75%). Colorless needles (from water), m.p. 141-143°. (According to patent data [5], 143°).

Heating of 0.2 g of the base with 0.4 g dimethyl sulfate at 100-110° for 4 hours gave the methiodide of 2,5-dimethyl-6-dimethylaminobenzothiazole. Yellow needles (from alcohol), m.p. 246-247° with decomposition.

Found %: I 36.84, 36.73. $C_{12}H_{17}N_2SI$. Calculated %: I 36.49.

m-Bromo-tert.butylbenzene was prepared, by analogy with m-bromotoluene [10], by bromination of p-acetamino-tert. butylbenzene [11] followed by saponification and deamination. m-Bromo-tert. butylbenzene was obtained in the form of a yellow oil with b.p. 237-239°, in agreement with the literature data [12]. Yield 36% calculated on p-acetamino-tert. butylbenzene.

3-Bromo-4,6-dinitro-tert. butylbenzene. 21.7 g 3-bromo-tert. butylbenzene was gradually added with stirring at the usual temperature to a mixture of 13 ml nitric acid (sp.gr. 1.5) and 30 ml concentrated sulfuric acid. The mixture was then stirred for 2 hours at 110-120° and poured into water. The solidified nitro product was filtered and recrystallized from alcohol. Cream-colored tablets with m.p. 92-94°. Yield 12.3 g (30.8%).

Found %: N 9.21, 9.07. $C_{10}H_{11}O_4N_2Br$. Calculated %: N 9.21.

2-Methyl-5-acetylamino-6-tert. butylbenzothiazole and 2-methyl-5-amino-6-tert. butylbenzothiazole (II) were prepared similarly from the methyl analogs. From 11 g 3-bromo-4,6-dinitro-tert. butylbenzene, by treatment with alcoholic Na_2S_2, was obtained 6.4 g (69%) of 2,2',4,4'-tetranitro-5,5'-ditert. butyldiphenyldisulfide. The disulfide was reduced with 27 g tin and 55 ml concentrated HCl. Boiling was continued for $3\frac{1}{2}$ hours after the tin had dissolved. The tin was precipitated with hydrogen sulfide, the filtrate was evaporated, and the dry residue boiled for an hour with 30 ml acetic anhydride. The excess of acetic anhydride was decomposed with water, and the solution was neutralized with ammonia; the filtered and dried precipitate was extracted with benzene. After recrystallization from benzene, 2-methyl-5-acetylamino-6-tert. butylbenzothiazole was obtained in the form of a yellowish, amorphous powder which gradually softened, without melting, at 150-170°, yield 1.8 g (27%).

Found %: N 10.54, 10.65. $C_{14}H_{18}ON_2S$. Calculated %: N 10.68.

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* All yields are stated in percentages of the theoretical.

** All the melting points and boiling points in this paper have been corrected.

TABLE 3

No.	Name of dye	Base	Alkylating agent	Ethyl orthoformate	Yield in % of theory	Gross formula	Nitrogen analysis, %	
							found	calc.
5	Bis-[3-ethyl-5-acetylamino-6-methylbenzothiazole (2)]-trimethinecyanine-p-toluenesulfonate	2,6-Dimethyl-5-acetylaminobenzothiazole 0.2 g	Ethyl p-toluene-sulfonate 0.14 g	0.4	14.5	$C_{34}H_{38}O_5N_4S_3$	8.15, 8.28	8.26
6	Bis-[3-methyl-5-acetylamino-6-tert. butylbenzothiazole (2)]-trimethinecyanine-p-toluenesulfonate	2-Methyl-5-acetylamino-6-tert.butylbenzothiazole 0.1 g	Methyl p-toluene-sulfonate 0.07 g	0.2	12	$C_{38}H_{46}O_5N_4S_3$	7.60, 7.41	7.63
16	Bis-[3,5-dimethyl-6-acetylaminobenzothiazole (2)]-trimethinecyanine-p-toluenesulfonate	2,5-Dimethyl-6-acetylaminobenzothiazole 0.2 g	Methyl p-toluene sulfonate 0.14 g	0.4	30.9 (unpurified)	$C_{32}H_{34}O_5N_4S_3$	Not isolated in pure state due to poor solubility	
17	Bis-[3-methyl-5-tert.butyl-6-acetylaminobenzothiazole (2)]-trimethine-cyanine-p-toluene-sulfonate	2-Methyl-5-tert.butyl-6-acetylaminobenzothiazole 0.1 g	Methyl p-toluene sulfonate 0.07 g	0.2	20.7	$C_{38}H_{46}O_5N_4S_3$	7.80, 7.77	7.63
11	Bis-[3,6-dimethylaminobenzothiazole (2)]-trimethinecyanine methosulfate	2,6-Dimethyl-5-aminobenzothiazole 0.2 g	Dimethyl sulfate 0.4 g	0.4	7.9	$C_{26}H_{34}O_4N_4S_3$	9.67, 9.73	9.96
12	Bis-[3-methyl-5-dimethylamino-6-tert.butylbenzothiazole (2)]-trimethinecyanine methosulfate	2-Methyl-5-amino-6-tert. butylbenzothiazole 0.1 g	Dimethyl sulfate 0.2 g	0.2	7	$C_{32}H_{46}O_4N_4S_3$	9.00, 8.85	8.81
22	Bis-[3,5-dimethyl-6-dimethylaminobenzothiazole (2)]-trimethinecyanine methosulfate	2,5-Dimethyl-6-aminobenzothiazole 0.2 g	Dimethyl sulfate 0.4 g	0.4	7.9	$C_{28}H_{34}O_4N_4S_3 \cdot 3H_2O$	9.10, 9.23 Presence of water of crystallization demonstrated	9.15
23	Bis-[3-methyl-5-tert. butyl-6-dimethylaminobenzothiazole (2)]-trimethine-cyanine methosulfate	2-Methyl-5-tert. butyl-6-aminobenzothiazole 0.2 g	Dimethyl sulfate 0.4 g	0.4	22.7	$C_{32}H_{46}O_4N_4S_3$	8.59, 8.54	8.81

1.5 g of the preceding compound was digested for 30 minutes with 30 ml dilute sulfuric acid. Neutralization with ammonia led to separation of 2-methyl-5-amino-6-tert. butylbenzothiazole. The product could only be recrystallized after purification by running the benzene solution through a column containing alumina. Colorless needles (from water), m.p. 126-127°. Yield 0.6 g (46%).

Found %: N 12.01, 12.03. $C_{12}H_{16}N_2S \cdot H_2O$. Calculated %: N 11.76.

Water of crystallization was found to be present.

2-Methyl-6-tert. butylbenzothiazole. p-Acetamino-tert. butylbenzene was nitrated [13], the acetamino group was saponified and the m-amino tert. butylbenzene was subjected to deamination, reduction of the nitro group and acetylation. The m-acetamino-tert. butylbenzene was again nitrated [13] and the acetyl group was saponified. 14.2 g of so-prepared 3-amino-4-nitro-tert. butylbenzene was dissolved in a mixture of 40 ml concentrated sulfuric acid and 60 ml water. The solution was diazotized and added dropwise to a boiling solution of Cu_2Br_2 while steam was passed through. 3-Bromo-4-nitro-tert.butylbenzene was distilled off in the form of an oil which was extracted with benzene and vacuum-distilled, b.p. 142-144°. Yield 10.2 g (54%). The preparation is not described in the literature.

10.2 g 3-bromo-4-nitro-tert. butylbenzene was dissolved in 25 ml alcohol and treated with a hot mixture of 6.1 g crystalline sodium sulfide, 0.9 g sulfur and 10 ml alcohol. After 2 hours' heating on the water bath, 2,2'-dinitro-4,4'-ditert.butyldiphenyldisulfide came down in the form of a viscous, yellow mass. The disulfide was separated from the liquid by decantation, washed with water and alcohol and dissolved by heating in 50 ml acetic acid. Into the cooled solution was gradually stirred 15 g zinc dust and 30 ml concentrated HCl. Stirring was continued for another hour and the solution was then filtered, diluted with water and saturated with sodium acetate. The white precipitate of the zinc mercaptide was filtered and dried, after which its weight was 3.5 g. It was boiled for an hour with 20 ml acetic anhydride. The excess of acetic anhydride was decomposed with water and the solution was made alkaline. The separated oil was extracted with benzene and vacuum-distilled. B.p. 134-136° at 15 mm. Yield 1.5 g or 44% calculated on the mercaptide.

Picrate: yellow powder, m.p. 137-139°.

Found %: N 12.96, 13.10. $C_{12}H_{15}NS \cdot C_6H_3O_7N_3$. Calculated %: N 12.90.

Methyl perchlorate: colorless needles (from alcohol), m.p. 210-211° with decomp.

Found %: Cl 10.85, 11.05. $C_{13}H_{18}O_4NSCl$. Calculated %: Cl 11.04.

The same preparation was obtained in the form of picrate by deamination of 2-methyl-5-amino-6-tert. butylbenzothiazole for the purpose of confirming the structure of the latter. 0.3 g amino compound was dissolved in 10 ml alcohol and 5 ml concentrated sulfuric acid was added. The mixture was cooled to 0° and diazotized with a solution of 0.2 g sodium nitrite in 2 ml water. The mixture was then heated on the water bath for 30 minutes, diluted with water, neutralized with sodium carbonate and extracted with ether. The oil remaining after distillation of the ether was dissolved in alcohol and mixed with an alcoholic solution of picric acid. After several recrystallizations from alcohol, a picrate with m.p. 137-139° was obtained. Yield 0.05 g. No m.p. depression of the mixture with the picrate of 2-methyl-6-tert. butylbenzothiazole prepared by the above-described method.

2-Methyl-5-tert.butylbenzothiazole was obtained in a similar manner to the above base. 22.5 g 3-nitro-4-amino-tert.butylbenzene [13] gave 14 g (47%) 3-nitro-4-bromo-tert.butylbenzene. A yellow oil, b.p. 174-175° (30 mm). According to the literature [14] 3-nitro-4-bromo-tert.butylbenzene boils at 124-126° (3 mm).

Treatment of 14 g of the nitrobromo derivative with alcoholic Na_2S_2 followed by reduction with zinc dust yielded 7.9 g of the corresponding zinc mercaptide, from which was obtained 3.3 g (49%, calculated on the mercaptide) 2-methyl-5-tert.butylbenzothiazole. Yellow oil, b.p. 153-156° (10 mm).

Picrate: yellow tablets, m.p. 147-149°.

Found %: N 12.78, 12.72. $C_{12}H_{15}NS \cdot C_6H_3O_7N_3$. Calculated %: N 12.90.

Methiodide: colorless needles (from alcohol), m.p. 228° with decomposition.

Found %: I 36.55, 36.79. $C_{13}H_{18}NSI$. Calculated %: I 36.60.

2,5-Dimethyl-6-nitrobenzothiazole (XII). 6 g 2,5-dimethylbenzothiazole [8] was added gradually at 20-25° to a mixture of 4.4 ml nitric acid (sp.gr. 1.4) and 12 ml concentrated sulfuric acid. The mixture was left for 15 minutes at room temperature and poured into water. The nitro product, weight 5.5 g (75%), came out in the form of a slightly yellowish precipitate, m.p. 105-112°. Repeated fractional crystallization from alcohol gave 1.9 g 2,5-dimethyl-6-nitrobenzothiazole. Cream-colored needles with m.p. 152-154°.

Found %: N 13.48, 13.30. $C_9H_8O_2N_2S$. Calculated %: N 13.46.

A second isomeric nitro product, isolated in quantity of 0.9 g, had m.p. 133-134°. In all probability it is 2,5-dimethyl-4-nitrobenzothiazole.

2-Methyl-5-tert.butyl-6-nitrobenzothiazole (XIII). 1.5 g 2-methyl-5-tert.butylbenzothiazole was gradually added to a mixture of 1.2 ml nitric acid (sp.gr. 1.4), and 3 ml concentrated sulfuric acid. The mixture was then heated and stirred for an hour at 90-100° and poured into water. The nitro product was filtered and recrystallized several times from alcohol. Cream-colored needles, m.p. 122-124°. Yield 0.7 g (40%).

Found %: N 10.91, 10.81. $C_{12}H_{14}O_2N_2S$. Calculated %: N 11.20.

2,5-Dimethyl-6-aminobenzothiazole (III) and 2,5-dimethyl-6-acetylaminobenzothiazole. 1.9 g 2,5-dimethyl-6-nitrobenzothiazole was mixed with a solution of 5.6 g stannous chloride in 15 ml concentrated HCl. The mixture was heated for 10 minutes at a gentle boil. After a few hours the precipitated double salt of the amine with stannous chloride was filtered and treated with excess caustic alkali. The amine was crystallized from benzene. Colorless needles, m.p. 167-168°; according to the patent data [9], the m.p. is 168°. Yield 1.5 g (94%). Treatment of 0.5 g amine with 2 ml acetic anhydride gave 0.5 g 2,5-dimethyl-6-acetylaminobenzothiazole. Colorless needles (from water), m.p. 226-228°.

Found %: N 12.41, 12.47. $C_{11}H_{12}ON_2S$. Calculated %: N 12.75.

Methiodide: colorless prisms (from alcohol), m.p. 261-262° with decomp.

Found %: I 35.25, 35.13. $C_{12}H_{15}ON_2SI$. Calculated %: I 35.08.

2-Methyl-5-tert.butyl-6-aminobenzothiazole (V) and 2-methyl-5-tert.butyl-6-acetylaminobenzothiazole were similarly prepared. Stannous chloride reduction of 0.5 g 2-methyl-5-tert.butyl-6-nitrobenzothiazole gave 0.4 g (90%) of the amino compound. Cream colored needles (from ligroin) m.p. 186-188°.

Found %: N 12.75. $C_{12}H_{16}N_2S$. Calculated %: N 12.73.

From 0.2 g amine was obtained 0.2 g 2-methyl-5-tert.butyl-6-acetylaminobenzothiazole. Colorless needles (from a mixture of 1 vol. benzene and 5 vols ligroin), m.p. 193-195°.

Found %: N 10.49, 10.39. $C_{14}H_{18}ON_2S$. Calculated %: N 10.68.

Dyes

Tetrasubstituted thiacarbocyanines

a) Dyes with dimethylamino groups were prepared in the following manner. 1 mole of the corresponding amino derivative of 2-methylbenzothiazole and 3 moles dimethyl sulfate were heated for 4 hours at 100-110°. Methylation of the amino group then took place at the same time as a quaternary salt was formed at the nitrogen atom of the thiazole ring. To the quaternary salt was added a few milliliters of pyridine and the equivalent amount of ethyl orthoformate. The mixture was boiled for 20 minutes, after which the pyridine was distilled off in vacuum; the dye was dissolved in chloroform and chromatographed several times on alumina. The dye isolated after the final chromatographic treatment was dissolved in 95% alcohol and filtered for removal of traces of alumina. After evaporation of the alcohol, the dye was isolated in the form of an amorphous powder. Dyes 11, 12, 22, 23 (Tables 1 and 2) were prepared in this manner.

b) Dyes with acetylamino groups. Quaternary salts were prepared by heating equivalent amounts of the corresponding acetylamino derivative of 2-methylbenzothiazole and the methyl (or ethyl) ester of p-toluenesulfonic acid at 130-140° for 1½-2 hours. Preparation and purification of the dyes were carried out as described above. The dyes 5, 6, 16 and 17 (Tables 1 and 2) were prepared in this manner. The yields and analytical data of the dyes are detailed in Table 3. The numbers assigned to the dyes correspond to their numbers in Tables 1 and 2. Yields of purified preparations are given in all cases, except for 16.

c) Dyes with amino groups. These were obtained by saponification of the acetyl groups in the acetylamino-substituted dyes. The unpurified dyes, prepared as described above, were boiled with 20% sulfuric acid for 20-30 minutes, after which the acid was neutralized with ammonia and the dye was filtered, dissolved in alcohol and the chloride of the dye precipitated with aqueous NaCl solution. The saponification could be performed by heating the dye for 20-30 minutes at 100-120° with a mixture of equal amounts of concentrated sulfuric acid and glacial acetic acid. After cooling, the solution was diluted with water and neutralized with ammonia. The following dyes were prepared in this way: bis-[3-ethyl-5-amino-6-methylbenzothiazole(2)]-trimethinecyanine chloride — 8 in table; bis-[3-methyl-5-amino-6-tert-butylbenzothiazole (2)]-trimethinecyanine chloride — 9; bis-[3,5-dimethyl-6-aminobenzothiazole (2)]-trimethinecyanine chloride —19; bis-[3-methyl-5-tert.butyl-6-aminobenzothiazole (2)]-trimethinecyanine chloride —20.

These four dyes have very poor solubility in alcohol and still worse in chloroform; purification by chromatography is therefore impossible. We were therefore unable to isolate them in the pure state. Only their absorption curves were investigated in alcoholic solutions of undetermined concentration.

Bis-[3-methyl-5-tert.butylbenzothiazole (2)]-trimethinecyanine chloride —3. 0.2 g 2-methyl-5-tert. butylbenzothiazole methiodide, 0.2 g ethyl orthoformate and 3 ml pyridine were boiled for 20 minutes. After cooling, the precipitated dye was filtered and crystallized from alcohol. Violet needles, m.p. 264-266°. Yield 0.07 g (44%).

Found %: I 22.23, 22,20. $C_{27}H_{33}N_2S_2I$. Calculated %: I 22.30.

Bis-[3-methyl-6-tert.butylbenzothiazole (2)]-trimethinecyanine perchlorate —14. 0.1 g 2-methyl-6-tert. butylbenzothiazole methyl perchlorate, 0.1 g ethyl orthoformate and 2 ml pyridine were boiled for 20 minutes. The dye was precipitated with ether, filtered and crystallized from alcohol. Violet needles, m.p. 263° with decomp. Yield 0.04 g (47%).

Found %: S 11.67, 11.40. $C_{27}H_{33}N_2O_4SCl$. Calculated %: S 11.66.

SUMMARY

1. The influence of steric hindrance on the auxochromic action of the dimethylamino group in tetra-substituted thiacarbocyanines was studied. It was established that the introduction of a methyl or a tertiary butyl group in the ortho-position to the dimethylamino group partly suppresses the latter's auxochromic action, the tertiary butyl group exerting a greater influence than the methyl group.

2. Nine new benzothiazole derivatives and fourteen new thiacarbocyanines were synthesized.

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INVESTIGATION OF THE STRUCTURE OF THE ALKALOID SONGORINE

PREPARATION OF ACONITANE – THE OXYGEN-FREE HETEROCYCLIC NUCLEUS OF SONGORINE

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A comparison of the compositions of various aconite alkaloids by A. P. Orekhov and R. A. Konovalova [1] led these authors to suggest that they are all derivatives of one and the same heterocyclic ring and only differ in the number and distribution of the substituents and in the presence of double bonds. The authors attempted to prepare such a heterocyclic ring of the alkaloid Talatisine, but the research did not lead to the desired result.

Some successes in the investigation of cyclic systems constituting the molecule of aconite alkaloids were achieved by using the method of selenium dehydrogenation. Hetisine, atisine, napelline and staphisine gave neutral fractions from which phenanthrene hydrocarbons were isolated [2]: from hetisine was got pimanthrene (1,7-dimethylphenanthrene); from atisine, 1-methylphenanthrene and 1-methyl-6-ethylphenanthrene; from staphisine, phenanthrene, pimanthrene and 3-methylretene (1,3-dimethyl-7-isopropylphenanthrene).

On the basis of the formation of phenanthrene homologs, in particular of pimanthrene and 3-methylretene, it was concluded that this group of alkaloids was related to the resin acids in the sense that the basis of the molecules of the aconite alkaloids is a pentacyclic structure, part of which is the perhydrophenanthrene ring condensed with a bicyclic, nitrogen-containing system.

In this paper we present the first results of our study of the structure of the alkaloid songorine, discovered by S. Yu. Yunusov [3].

Songorine $C_{21}H_{29}O_3N$ contains two hydroxyl and one carbonyl group; it has a double bond. From the standpoint that it was first necessary to establish the nature and location in the molecule of the rings in which the nitrogen atom is linked, we started our investigation with the aim of preparing the oxygen-free heterocyclic ring of the alkaloid in order to be able subsequently to effect its Hofmann degradation and to investigate the unsaturated nitrogen-free substance.

Songorine with m.p. 201-202° and specific rotation $[\alpha]_D$ −135.4° was prepared from Aconitum songoricum. Its constants correspond to those in the literature. The hydroxyl groups of songorine were replaced by chlorine by reaction with phosphorus oxychloride. The chlorine derivative (without purification and isolation in the individual state) was subjected to catalytic reduction with skeletal nickel catalyst at a small excess pressure of hydrogen in presence of two equivalents of caustic alkali. An amino ketone was obtained with the composition $C_{21}H_{31}ON$ for which we propose the name of oxoaconitane. The base is a colorless crystalline substance with m.p. 64-66°; its hydrochloride has the composition $C_{21}H_{31}ON \cdot HCl$, m.p. 293°; $[\alpha]_D$ −76.9°; hydrobromide $C_{21}H_{31}ON \cdot HBr$, m.p. 299°, $[\alpha]_D$ −69.7°. Both salts are well-crystallized, soluble in alcohol, poorly soluble in acetone and water.

The carbonyl group of oxoaconitane was reduced by $LiAlH_4$ to give the amino alcohol hydroxyaconitane $C_{21}H_{33}ON$, m.p. 151.5°; $[\alpha]_D$ −38.6°.

Elimination of the hydroxy group of hydroxyaconitane with formation of the oxygen-free substance $C_{21}H_{33}N$ was effected as in the removal of the hydroxy groups from songorine: substitution with chlorine by the action of phosphorous oxychloride followed by reduction over skeletal nickel catalyst.

Aconitane is the saturated, oxygen-free heterocyclic nucleus of the alkaloid songorine. The base $C_{21}H_{33}N$ melts at 69.5-70°, rotates the plane of polarization of light to the left ($[\alpha]_D$ −50.3°), and distils in vacuum at 170-180° (3 mm). Aconitane hydrochloride has the composition $C_{21}H_{33}N \cdot HCl$, m.p. 275°, $[\alpha]_D$ −37.2°. Hydrobromide $C_{21}H_{33}N \cdot HBr$, m.p. 282-283°, $[\alpha]_D$ −29.4°.

EXPERIMENTAL

(assisted by R. I. Bogomazova)

Preparation of Oxoaconitane

To 10 g songorine with ice cooling was added 100 ml phosphorus oxychloride. The reaction mass was gradually brought to the boil over a gauze and boiled for 2 hours, after which the excess of phosphorus oxychloride was distilled off in vacuum. The residue was treated with water, at first with ice cooling and later while heating on the boiling water bath and being intensively shaken until solution was complete. The aqueous solution was made alkaline with concentrated aqueous ammonia and extracted with ether. The ether extract was dried with potassium carbonate and the ether was distilled off to leave 10.5 g of a colorless oil which was dissolved in 300 ml 80% ethyl alcohol. To the alcoholic solution was added 6 ml 40% NaOH solution and 15 g skeletal nickel catalyst, and the whole was shaken under slight excess pressure in a hydrogen atmosphere. In the course of 16 hours 1750 ml (2.7 moles) hydrogen was absorbed, after which absorption ceased. The solution was filtered from catalyst, acidified with hydrochloric acid and evaporated in a vacuum. Addition of water to the oily residue brought down oxoaconitane hydrochloride which was sparingly soluble in water and after recrystallization from water weighed 2.8 g and melted at 293°. After a second crystallization the yield was 1.7 g with the same melting point.

0.0819 g substance in 10 ml 0.5% HCl, l = 1 dm, α_D −0.63°, $[\alpha]_D$ −76.9°.

3.879 mg substance: 10.349 mg CO_2; 3.163 mg H_2O. 10.172 mg substance: 0.353 ml N_2 (24°, 729 mm). Found %: C 72.94; H 9.12; N 3.82. $C_{21}H_{31}ON \cdot HCl$. Calculated %: C 72.06; H 9.22; N 4.02.

The base was prepared by stirring 1.7 g of the hydrochloride with water, making the suspension alkaline with aqueous ammonia and extracting with ether. The ether extract was dried with potassium carbonate and the ether was driven off to leave the colorless crystalline base, m.p. 64-66°, readily soluble in ether, pentane, alcohol, acetone, chloroform and benzene; sparingly soluble in water. The substance could not be recrystallized. The hydrobromide of oxoaconitane was prepared in the form of fine needlets by triturating the base with 5% aqueous HBr and crystallizing from hot alcohol with addition of an equal volume of ether. M.p. 299°. 0.1019 g substance in 10 ml water, l = 1 dm, α_D −0.71°, $[\alpha]_D$ −69.7°.

3.372 mg substance: 7.960 mg CO_2; 2.501 mg H_2O. 3.392 mg substance: 7.996 mg CO_2; 2.539 mg H_2O. 10.281 mg substance: 0.295 ml N_2 (23°, 740 mm). 10.890 mg substance: 0.309 ml N_2 (23°, 738 mm). 4.542 mg substance: 2.191 mg AgBr. Found %: C 64.42, 64.33; H 8.30, 8.37; N 3.22, 3.18; Br 20.53. $C_{21}H_{31}ON \cdot HBr$. Calculated %: C 63.95; H 8.18; N 3.55; Br 20.26.

The mother liquor from the hydrochloride of the base was made alkaline with aqueous ammonia and extracted with ether. After drying the ether extract with potassium carbonate and driving off the ether, 6.0 g of colorless oil was obtained from which we only succeeded in isolating oxoaconitane by chromatography: 6 g of the substance in 60 ml ether; solution passed through a column containing a bed of 75 g activated alumina moistened with wet ether; height of bed 70 cm. After passage of the whole of the solution, the sorbent in the column was washed with ether. From the instant of commencement of emergence of the bases from the column, determined by the reaction with silicotungstic acid, 30 ml fractions of eluate were collected. Distillation of the solvent from the second to the fourth fractions gave 2.1 g crystallizable substance, trituration of which with 5% aqueous HBr gave 1.8 g crystalline hydrobromide melting at 298° (from alcohol-ether) and not causing a melting point depression in admixture with the previously isolated hydrobromide of oxoaconitane. 0.1077 g substance: 10 ml water, l = 1 dm, α_D −0.75 $[\alpha]_D$ −69.6°.

Preparation of Hydroxyaconitane

2.5 g oxoaconitane and 1.0 g $LiAlH_4$ were dissolved in 800 ml absolute ether and refluxed four hours. The solvent was then distilled off to the extent of two-thirds of its volume; the reaction mass was treated with 10% aqueous HCl until the precipitate formed at the start of the addition had redissolved; the aqueous acid layer was separated; the ether layer was extracted 3 times with 10% HCl. The aqueous acid extracts were combined, made alkaline with 40% NaOH and extracted with ether. Drying of the ether extract with potassium carbonate and distillation of the solvent gave 2.35 g partly crystallizing residue which was treated with pentane. The oil then went into solution, leaving a residue of colorless needles. The latter were drained and further purified by crystallization from acetone and then from alcohol. Yield 0.9 g colorless needles melting at 151.5-153°. 0.0881 g substance: 10 ml alcohol, l = 1 dm, α_D −0.34, $[\alpha]_D$ −38.6°.

4.064 mg substance: 12.049 mg CO_2; 3.740 mg H_2O. 10.567 mg substance: 0.395 ml N_2 (24° 738 mm). Found %: C 80.91; H 10.30; N 4.17. $C_{21}H_{33}ON$. Calculated %: C 79.94; H 10.54; N 4.44. 0.0113 g substance: 0.0989 g camphor: Δt 15.0 and 14.0° in two experiments. Found: M 305 and 327. $C_{21}H_{33}ON$. Calculated: M 315.

Preparation of Aconitane

To 0.8 g hydroxyaconitane, with ice cooling, was added 8 ml phosphorus oxychloride; the reaction mass was gradually brought to the boil on a gauze and refluxed 2 hours. The excess of phosphorus oxychloride was distilled off in vacuum and the residue was worked up with water, at first with ice-cooling and then on the boiling water bath; the oil was seen to dissolve and a colorless crystalline substance came out. The suspension was made alkaline with aqueous ammonia and extracted with ether. After drying the extract with potassium carbonate and distilling off the ether, a slightly colored liquid base was obtained which was dissolved in 80 ml alcohol. To the alcoholic solution was added 1.5 g skeletal nickel catalyst and the whole was shaken at a slight excess pressure in a hydrogen atmosphere. Absorption was completed in 8 hours. The alcoholic solution was filtered from catalyst, acidified with hydrochloric acid and evaporated in vacuum. The colorless crystalline residue of the hydrochloride was recrystallized by adding ether to its alcoholic solution. Yield 0.5 g fine, colorless needles, melting at 275° with partial sublimation. 0.0915 g substance: 10 ml alcohol, $\underline{l}$ = 1 dm, α_D −0.34°, $[\alpha]_D$ −37.2°.

The specific rotation did not change after recrystallization.

3.557 mg substance: 9.733 mg CO_2; 3.110 mg H_2O. 3.318 mg substance: 9.104 mg CO_2; 2.958 mg H_2O. 8.500 mg substance: 0.304 mg N_2 (26°, 725 mm). 8.498 mg substance: 0.295 ml N_2 (26°, 725 mm). Found %: C 74.67, 74.88; H 9.78, 9.97; N 3.89, 3.78. $C_{21}H_{33}N \cdot HCl$. Calculated %: C 75.05; H 10.20; N 4.17.

The base was obtained by treating the aqueous solution of the hydrochloride with aqueous ammonia and extracting with ether. After drying the extract with potassium carbonate and driving off the solvent, oily base was obtained which crystallized when rubbed with a glass rod. Crystallization from acetone gave colorless needles melting at 69.5-70°. The m.p. was unchanged after recrystallization. The compound is readily soluble in pentane, benzene, ether, chloroform; less readily soluble in alcohol and acetone, poorly soluble in water; it distils in vacuum without decomposition at 170-180° (3 mm). 9.540 mg substance: 1 ml alcohol, $\underline{l}$ = 0.5 dm, α_D −0.24°, $[\alpha]_D$ −50.3°.

4.053 mg substance: 12.608 mg CO_2; 4.058 mg H_2O. 4.921 mg substance: 15.241 mg CO_2; 4.916 mg H_2O. 8.750 mg substance: 0.331 mg N_2 (26°, 735 mm). 8.704 mg substance: 0.353 ml N_2 (26°, 735 mm). Found %: C 84.89, 84.52; H 11.20, 11.18; N 4.17, 4.47. $C_{21}H_{33}N$. Calculated %: C 84.21; H 11.11; N 4.68. 4.460 mg substance; 59.5 mg camphor: Δt 10.5 and 10.0° in two experiments. Found: M 286 and 300. $C_{21}H_{33}N$. Calculated: M 299.

The hydrobromide was obtained by triturating the base with 5% aqueous HBr. After recrystallization from alcohol-ether, the salt melted at 282-283°; no change after a second crystallization.

10.021 mg substance: 1 ml alcohol, $\underline{l}$ = 0.5 dm, α_D −0.15°, $[\alpha]_D$ −29.4°.

3.882 mg substance: 9.533 mg CO_2; 3.030 mg H_2O. 4.195 mg substance: 10.300 mg CO_2; 3.311 mg H_2O. 9.085 mg substance: 0.307 ml N_2 (26°, 732 mm). 10.415 mg substance: 0.324 ml N_2 (26°, 732 mm). Found %: C 67.01, 67.00; H 8.73, 8.83; N 3.71, 3.42. $C_{21}H_{33}N \cdot HBr$. Calculated %: C 66.30; H 9.00; N 3.68.

SUMMARY

From songorine $C_{21}H_{29}O_3N$ were prepared the previously unknown amino ketone oxoaconitane $C_{21}H_{31}ON$, the amino alcohol hydroxyaconitane $C_{21}H_{33}ON$ and the oxygen-free substance aconitane $C_{21}H_{33}N$.

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THE STRUCTURE OF THE POLYAMIDES OF DIPHENIC ACID

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The polyamides formed by diphenic acid and hexamethylenetetramine are transparent, light-yellow resins, soluble in m-cresol, alcohol-benzene and glacial acetic acid. The resins with a molecular weight of 10,000 have a m.p. of 170-175°. Due to the fact that the structure of high-molecular compounds considerably influences their physical properties, it was of interest to establish to what extent the molecular chains of polyamide prepared from diphenic acid and hexamethylenetetramine were oriented. For the purpose of studying the polyamide structure, polyhexamethylenediphenamide and (for comparison) polyhexamethyleneadipamide were synthesized.

The reaction conditions for the preparation of polyhexamethylenediphenamide were as follows: The neutral salt of diphenic acid and hexamethylenediamine was placed in a flask heated on a metal bath. The bath temperature was regulated by a contact thermometer and checked by a mercury thermometer immersed in the reaction mixture. The reaction was performed at a temperature of 220° for 2 hours under a reflux condenser, then for four hours without the condenser while distilling off reaction products, and for two hours in a 10-15 mm vacuum at the same temperature. Nitrogen (purified from oxygen traces) was passed through the reaction mixture during the experiment.

Polyhexamethyleneadipamide was synthesized by the known procedure.*

The prepared polyhexamethylenediphenamide had m.p. 170-175°; the polyhexamethyleneadipamide had m.p. 248-250°.

Filaments with a diameter of about 1 mm were drawn out from the polyamides and X-ray diagrams were prepared,** using a "Mikro" apparatus. Exposure 50 milliampere hours.

Double-sided Debyeograms were obtained, on which could be measured the distances (21) between symmetrically distributed diffraction patterns. Knowing the radius of the cylindrical camera (2R = 57.4 mm), we could determine, from the measured distances, the deviation angle θ for each diffraction pattern ($\theta = \underline{1}/2R$). From these angles was determined the value (d) of the interplanar distances (for the Debye lines) or the mean distance (d') between the scattering centers (for diffusion haloes) by the usual formula (for $\lambda = 1.537$ A).

The X-ray diagram prepared from polyhexamethylenediphenamide contains only diffusion haloes characterized by the magnitudes presented in Table 1.

The X-ray diagram prepared from hexamethyleneadipamide contains, apart from diffusion haloes one of which is resolved into two very similar independent haloes, four relatively weak and diffuse Debye lines. The data characterizing these haloes are set out in Table 2.

TABLE 1

θ	d^1 (A)	Maximum error Δd (A) with a measuring error of ± 0.2 mm
6°00'	7.361	0.25
10°31'	4.216	0.12
21°24'	2.109	0.018

The data that have been obtained show that polyhexamethylenediphenamide has a definitely amorphous structure. This amorphous structure is evidently due to the distribution of the carboxyl groups in diphenic acid not being favorable to orientation of the polyamide chains.

The X-Ray diagrams of the polyamides are shown in Figures 1 and 2.

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* See V. V. Korshak and S. R. Rafikov. Synthesis and Investigation of High-Molecular Compounds, p. 240 (1949).

** The X-ray work was carried out in the laboratory of physical metallurgy by Doctor V. I. Arkharov and assistant Z. P. Kichigina to whom we convey our thanks.

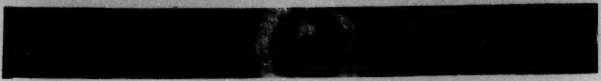

Fig. 1. X-Ray diagram of polyhexamethylenediphenamide.

Fig. 2. X-Ray diagram of polyhexamethylenedipamide.

TABLE 2

θ	d	Intensity and diffusivity
6°22'	6.939	Moderate
10°00'	4.431	Very strong diffusion
11°59'	3.705	Very strong diffusion
18°56'	2.372	Weak
20°48'	2.167	Weak, strongly diffused
22°45'	1.990	Very weak, strongly diffused
31°27'	1.475	Very weak, strongly diffused
40°03'	1.196	Very weak, strongly diffused

SUMMARY

It has been established that polyhexamethylenediphenamide possesses an amorphous structure.

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SYNTHESIS OF DERIVATIVES OF 3,4'-ACE-1,2-BENZANTHRACENE WITH THE HELP OF LITHIUM REAGENTS

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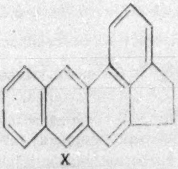
Homologs of 3,4'-ace-1,2-benzanthracene are of interest because of their ability to induce malignant neoplasms [1]; one of us synthesized them [2] by reaction of organomagnesium compounds with 3,4'-ace-1,2-benzanthrone-10. The yields of hydrocarbons did not exceed 21-30% of the theoretical by this route.

In the present communication we describe a method of preparation of alkyl and other functional derivatives of 3,4'-ace-1,2-benzanthracene with substituents in the 10-position, based on the use of organolithium compounds [3]. The starting organolithium compound of 3,4'-ace-1,2-benzanthracene, which readily exchanges the metal for diverse radicals, is smoothly prepared by the action of n-butyllithium or of phenyllithium on 10-bromo-3,4'-ace-1,2-benzanthracene.

Replacement of bromine by lithium in 10-bromo-3,4'-ace-1,2-benzanthracene proceeds much more slowly with phenyllithium than with n-butyllithium. In the former case the reaction is completed after an hour, whereas with n-butyllithium it is completed in a few minutes.

The reaction between 3,4'-ace-1,2-benzanthryl-10-lithium and alkyl halides proceeds more or less readily depending on their nature. The reaction proceeds the most readily with methyl iodide, giving 10-methyl-3,4'-ace-1,2-benzanthracene (I) in 72% yield. Reaction between 3,4'-ace-1,2-benzanthryl-10-lithium and higher alkyl halides (ethyl iodide and n-butyl iodide) proceeds much more slowly and calls for heating for about 40 hours at 40° in order to complete it (II and III).

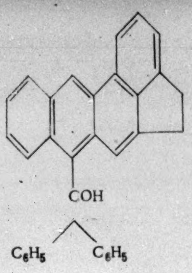
In the carboxylation of 3,4'-ace,1,2-benzanthryl-10-lithium prepared with the help of n-butyllithium or phenyllithium, from 8 to 20% of the 3,4'-ace-1,2-benzanthracene is recovered unchanged side by side with the carboxylic acid (IV) (40% yield). It was established that the hydrocarbon is formed during the very process of carboxylation and is not a consequence of reaction between the organolithium compound and the ether, toward which 3,4'-ace,1,2-benzanthryl-10-lithium is very stable.



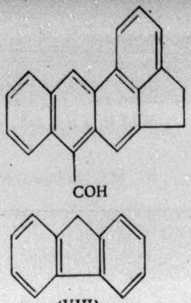
X = CH_3 (I); C_2H_5 (II), n-C_4H_9 (III), COOH (IV), $COOC_2H_5$ (V), CH_2CH_2OH (VI).

Reaction of the starting organolithium compound with ethyl chloroformate or ethylene oxide gives the corresponding ethyl ester of 3,4'-ace-1,2-benzanthracene-10-carboxylic acid (V) and 10-β-hydroxyethyl-3,4'-ace-1,2-benzanthracene (VI).

With non-enolizing ketones the lithium compound of 3,4'-ace-1,2-benzanthracene gives tertiary alcohols. Benzophenone gave 3,4'-ace,1,2-benzanthryl-10-diphenylcarbinol (VII); fluorenone gave 3,4'-ace-1,2-benzanthryl-10-fluorenol (VIII):



(VII)



(VIII)

EXPERIMENTAL

10-Methyl-3,4'-ace-1,2-benzanthracene (I). To an ethereal solution of n-butyllithium, prepared by the usual method [3] from 0.5 g n-butyl chloride, 0.1 g metallic lithium and 10 ml absolute ether, is added a solution of 1 g of 10-bromo-3,4'-ace,1,2-benzanthracene in 15 ml dry benzene (thiophene-free). After 10 minutes, addition is made to the reaction mass of an ethereal solution of 1.3 g methyl iodide. The mass is heated for 2 hours at 40° and treated with water; the solvents are distilled off and the crystalline residue is twice recrystallized from a mixture of benzene and ethanol to give 0.58 g light-yellow crystals melting at 181-182° and not depressing the melting point of a specimen of 10-methyl-3,4'-ace,1,2-benzanthracene prepared by another route [2]. Yield 72.5% of the theoretical.

10-Ethyl-3,4'-ace-1,2-benzanthracene (II). To 3,4'-ace-1,2-benzanthryl-10-lithium, prepared by the above-described method from 1 g of the bromo-compound, was added 1.4 g ethyl iodide, and the reaction mass was heated for 40 hours at 40°.

After the reaction mixture had been worked up in the usual way, the ether-benzene layer yielded a resinous product from which was obtained, by crystallization from benzene-petroleum ether, 0.34 g substance melting at 168-171° (40.1% of theory).

After a fresh crystallization from the same solvents, the m.p. was 174-175° and there was no depression in admixture with a specimen of 10-ethyl-3,4'-ace-1,2-benzanthracene [2]. 3,4'-Ace-1,2-benzanthracene was not detected among the reaction products.

Heating for 3 hours gave 13% of 10-ethyl-3,4'-ace-1,2-benzanthracene.

10-n-Butyl-3,4'-ace-1,2-benzanthracene (III). To 3,4'-ace-1,2-benzanthryl-10-lithium, prepared from 1 g 10-bromo-3,4'-ace-1,2-benzanthracene, was added 2.5 g n-butyl iodide. The mixture was heated for 40 hours at 40°. From the reaction products was isolated a hydrocarbon (0.57 g) with m.p. 122-128° (60.3% of the theoretical). After recrystallization from benzene-ethanol, the substance melted at 127-128° and did not depress the m.p. in admixture with a specimen of 10-n-butyl-3,4'-ace-1,2-benzathracene [2]. When the reaction period was cut down to 20 hours, the products isolated were 0.19 g 10-n-butyl-3,4'-ace-1,2-benzanthracene with m.p. 121-130° (41% of the theoretical) and 0.05 g 3,4'-ace-1,2-benzanthracene (13%), formed by hydrolysis of the original organolithium compound not entering into reaction.

3,4'-Ace-1,2-benzanthracene-10-carboxylic acid (IV).

a) Using n-butyllithium. To an ethereal solution of n-butyllithium, prepared from 0.5 g n-butyl chloride and 0.1 g lithium metal, was added a benzene solution of 1 g 10-bromo-3,4'-ace-1,2-benzanthracene (15 ml). After 10 minutes the reaction mixture was poured on to solid carbon dioxide, then water was added, and the precipitate was filtered and treated with hot caustic alkali solution; the alkaline filtrate was combined with the main aqueous layer. Acidification yielded 0.52 g 3,4'-ace-1,2-benzanthracene-10-carboxylic acid, melting at 229-230° (with decomp.). Yield 58.2% of the theoretical.

After crystallization from ethanol, the acid forms long, yellow needles melting at 236-237° (with decomposition).

5.257 mg substance: 16.304 mg CO_2; 2.304 mg H_2O. Found %: C 84.63; H 4.90. $C_{21}H_{14}O_2$. Calculated %: C 84.54; H 4.73.

From the ether-benzene layer was separated 0.03 g of a light-yellow, crystalline substance which after crystallization from benzene had m.p. 191-192° and did not depress the m.p. in admixture with 3,4'-ace-1,2-benzanthracene.

b) Using phenyllithium. To an ethereal solution of phenyllithium (0.002 mole) was added a benzene solution of 0.5 10-bromo-3,4'-ace-1,2-benzanthracene (0.0015 mole). After reaction for 10 minutes, the products of reaction were carboxylated by the usual method. 0.05 g 3,4'-ace-1,2-benzanthracene-10-carboxylic acid (11% of theory) and 0.33 g of the original bromo compound (60% of the amount taken) were obtained. On increasing the duration of reaction to 1½ hours, the yields were 0.19 g acid (42.7% of theory) and 0.08 g 3,4'-ace-1,2-benzanthracene (21% of theory).

The same results were obtained when the duration of the reaction between phenyllithium and the bromo compound was raised to 3-5 hours. Nor did the picture change when the amount of phenyllithium was increased to 3 equivalents.

Ethyl ester of 3,4'-ace-1,2-benzanthracene-10-carboxylic acid (V). Reaction of an ether-benzene solution of 3,4'-ace-1,2-benzanthryl-10-lithium, prepared from 0.5 g 10-bromo-3,4'-ace-1,2-benzanthracene and n-butyllithium, with 0.2 g ethyl monochloroformate gave a yellow crystalline product, melting after crystallization from a mixture of benzene and petroleum ether at 161-177°. After recrystallization from the same solvents, 0.26 g of the ethyl ester of 3,4'-ace-1,2-benzanthracene-10-carboxylic acid was obtained with m.p. 180.2-182.5° (yield 53.5% of the theoretical). After one more recrystallization the compound melted at 182.5-184.5°.

4.462 mg substance: 13.823 mg CO_2; 2.300 mg H_2O. Found %: C 84.54; H 5.76. $C_{23}H_{18}O_2$. Calculated %: C 84.66; H 5.52.

From the main mother liquor was isolated 0.025 g 3,4'-ace-1,2-benzanthracene (m.p. 189-191°).

10-β-Hydroxyethyl-3,4'-ace-1,2-benzanthracene (VI). Into an ether-benzene solution of 3,4'-ace- 1,2-benzanthryl-10-lithium, prepared from 1 g 10-bromo-3,4'-ace-1,2-benzanthracene, was passed an excess of gaseous ethylene oxide. Heat was developed and a white, flocculent precipitate of lithium alcoholate was formed. The latter was decomposed and 0.44 g of a substance with m.p. 187.5-189° was filtered off. The ether-benzene solution yielded 0.19 g substance with m.p. 184-187°. Crystallization of the combined precipitates from ethylacetoacetate gave 0.56 g (63% of the theoretical) of 10-β-hydroxyethyl-3,4'-ace-1,2-benzanthracene in the form of yellow, fluffy needlets melting at 189.5-190.5°.

3.888 mg substance: 12.614 mg CO_2; 2.139 mg H_2O. Found %: C 88.53; H 6.15. $C_{22}H_{18}O$. Calculated %: C 88.56; H 6.08.

3,4'-Ace-1,2-benzanthryl-10-diphenylcarbinol (VII). To an ether-benzene solution of 3,4'-ace-1,2-benzanthryl-10-lithium, prepared from 1 g 10-bromo-3,4'-ace-1,2-benzanthracene and n-butyllithium, was added 0.55 g benzophenone. After 2 hours, water was added to the reaction mixture, the solvents were distilled off and the residue crystallized from isoamyl ether, to give 0.84 g yellow powder, melting at 189-192° (with decomp.). Yield 64.1% of the theoretical.

Recrystallization from the same solvent gave 0.50 g 3,4'-ace-1,2-benzanthryl-10-diphenylcarbinol in the form of long prisms melting at 193-193.5° (with decomp.).

7.312 mg substance: 24.306 mg CO_2; 3.720 mg H_2O. Found %: C 90.71; H 5.69. $C_{33}H_{24}O$. Calculated %: C 90.78; H 5.54.

3,4'-Ace-1,2-benzanthryl-10-fluorenol (VIII). To a solution of 3,4'-ace-1,2-benzanthryl-10-lithium, prepared from 0.5 g 10-bromo-3,4'-ace-1,2-benzanthracene and n-butyllithium, was added an ethereal solution of 0.28 g fluorenone. Slight heat was developed and the color became lighter. After working up as usual, the oily residue was crystallized from isoamyl ether. 0.46 g yellow powder with m.p. 230-231° was isolated, representing 70.7% of the theoretical yield. After two crystallizations from acetone it formed stout, light-yellow needles of 3,4'-ace-1,2-benzanthryl-10-fluorenol, melting at 234.5-235°.

5.814 mg substance: 19.430 mg CO_2; 2.681 mg H_2O. Found %: C 91.20; H 5.16. $C_{33}H_{22}O$. Calculated %: C 91.21; H 5.10.

SUMMARY

Reaction of n-butyllithium or phenyllithium with 10-bromo-3,4'-ace-1,2-benzanthracene gives 3,4'-ace-1,2-benzanthryl-10-lithium, which can be successfully used for synthesis of homologs and oxygenated derivatives of 3,4'-ace-1,2-benzanthracene.

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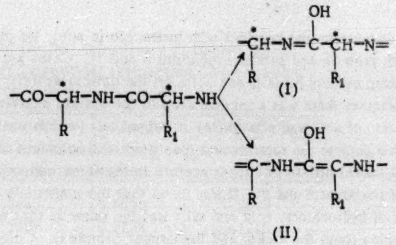
SPECTROPHOTOMETRY OF BIURET COMPLEXES AS A METHOD OF INVESTIGATION OF PROTEINS AND PEPTIDES

XVII. DIRECTION OF ENOLIZATION DURING THE BIURET REACTION OF PROTEINS AND PEPTIDES

M. I. Plekhan and N. D. Russianova

The necessity for a strongly alkaline medium for the formation of biuret complexes gives reason to believe that enolization must occur in this reaction. This is supported by Rising's observation [1] that substituted phthalimide and succinimide, in which there is no possibility of enolization, do not form a biuret complex. But whereas in the case of diamides and imino acids only one direction of enolization is possible, there are two possible directions of the reaction with peptides and proteins:



Although Rising ruled out the possibility of the N-enolic form of the peptide bond in the structure of the biuret complex of triglycylglycine, he did not experimentally demonstrate the correctness of this hypothesis.

Since we considered the N-enolic form of the peptide bonds to be the most probable in the biuret reaction of peptides and proteins, we considered an experimental proof of this feature of the structure of the complex desirable.

1. Effect of the Biuret Reaction on the Optical Activity of Peptides and Protein

On comparing formulas (I) and (II) we can observe that carbon-carbon enolization (direction II) must lead to loss of the optical activity of a polypeptide and protein. On the other hand, enolization of the peptide bond in accordance with scheme I does not modify the optical activity of the substance. In the light of these considerations we based our investigations on a study of the optical activity of synthetic polypeptides and proteins during formation of the biuret complexes. As synthetic models we used optically active alanine di- and tripeptides which were synthesized essentially by Bergman's method. (Details in experimental part). Proteins taken for investigation were casein, gelatin and serum albumen. 1% solutions of proteins and peptides were prepared and the rotation of the plane of polarization by these solutions was measured. Solutions of the copper and nickel biuret complexes were also prepared. In the case of the nickel complexes, the rotation measurements were performed on the solutions of the complexes themselves. The solutions of the copper complexes were so intensely colored that they were not amenable to measurement, and the rotation was determined after breakdown of the complex by acidification.

Results presented in Table 1. The following points emerge on examining the data of this table:

1) Formation of nickel biuret complexes both by proteins and polypeptides in the majority of cases does not change the magnitude of the rotation of the plane of polarization (column 4). The rotation of the nickel biuret complex of the alanine tripeptide is higher than the rotation of the free alanine tripeptide. The insignificant fall in the rotation of the solution of the casein complex is within the limit of experimental error.

2) Formation of a complex contributes to the constancy of the optical activity of proteins and peptides and hinders racemization under the influence of alkalies. Even after standing for 24 hours the rotation of solutions of biuret complexes of proteins and peptides does not change (column 4). On the other hand, after standing with alkali for 24 hours, the solutions of the free proteins and peptides undergo considerable racemization (column 3).

TABLE 1

Optical Activity of Peptides and Proteins after Formation of Biuret Complexes

Substance examined	1 Conc. of solution (%)	2 Rotation of solution $[\alpha]_D^{20}$	3 Rotation of solution with addition of alkali after 24 hours	4 Rotation of Ni-biuret complex of the substance after	
				2 hours	24 hours
Casein	1	−1.15	−0.65	−0.95	−0.98
Gelatin	1	−1.4	−0.75	−1.4	−1.45
Serum albumen	1	−0.67	−0.5	−0.62	−0.62
Carbobenzoxy-l-alanyl-l-alanine	1.5	−0.62	−0.4	−0.6	−0.6
l-Alanyl-l-alanine	2	−0.5	−0.35	−0.55	−0.55
Carbobenzoxy-l-alanyl-l-alanyl-l-alanine	1	−0.75	−0.51	−0.98	−0.98
l-Alanyl-l-alanyl-l-alanine	1.25	−0.58	−0.38	−1.0	−1.0

3) After decomposing the biuret complexes of proteins and peptides with hydrochloric acid, we observed a considerable decline of the optical activity of both proteins and peptides (columns 5 and 7). Cases are reported in the literature of a considerable effect being exerted by salts and acids on the optical activity of protein solutions [2,3]. It was necessary to check whether there was a marked drop in the optical activity of solutions of proteins and peptides as a result of addition of acid and of a nickel or copper salt (which was formed after decomposition of the complex). For this purpose the rotation was measured with solutions of free proteins with additions of hydrochloric acid and nickel nitrate or copper acetate in the same concentration as was present after decomposition of the complexes (columns 6 and 8). It was found that the magnitude of the rotation with solutions of proteins with additions of hydrochloric acid and salts was the same as that with solutions of proteins after decomposition of the complex (both the nickel and the copper complex). Consequently the fall in rotation with protein solutions observed after decomposition of the complex is the result of addition of hydrochloric acid and the formation of a salt, and is not the result of racemization.

All the above observations lead indisputably to the conclusion that racemization does not take place during the biuret reaction of proteins and peptides and that consequently, enolization of the peptide bonds occurs. We are therefore justified in representing the peptide bonds in the enol form in the structure of the biuret complex of proteins and peptides.

2. Influence of Optical Isomerism of Peptides on the Formation of the Biuret Complex

In a previous communication one of us showed the influence of various amino acids on the character of the complex formation of peptides. But the question of the influence of the optical isomerism of amino acids on the biuret reaction of peptides has not previously been considered. In view of the fact that natural compounds contain optically active amino acids, it is necessary to establish whether the optical activity of the amino acids also has some influence on the character of complex formation of peptides. With this aim we synthesized alanine di- and tripeptides into whose composition entered both the natural l-form of alanine and the synthetic d-form. For comparison, we also synthesized the racemic alanine di- and tripeptides.

In Tables 2 and 3 and Figures 1 and 2 are presented the results of spectrophotometric measurements of high absorption by the copper biuret complexes of alanine di- and tripeptides.

Table 2 and Fig. 1 show that the character of the absorption of the complex of the racemic tripeptide is similar to the absorption of optically active l-alanyl-l-alanyl-l-alanine and of the tripeptide containing the d-form (l-alanyl-d-alanyl-l-alanine). The position of the maximum in all three complexes is at one and the same wave-length of 570 mμ. The intensity of absorption throughout the whole of the visible portion of the spectrum is very similar in all three complexes.

The spectrophotometric investigation of the light absorption by complexes of alanyl dipeptides and their carbobenzoxy derivatives showed that the complex of the optically active l-alanyl-l-alanine has an absorption character very similar to that observed by us for the complex of racemic alanylalanine. The absorption maximum with complexes of alanyl dipeptides lies at a wave-length of 680 mμ, and with complexes of the carbobenzoxy derivatives of 660 mμ. The results provide evidence that the character of the absorption in the visible region

5	6	7	8
Rotation after breakown of Ni-complex	Rotation of test solution with addition of Ni(NO$_3$)$_2$ and HCl	Rotation after breakdown of Cu-biuret complex	Rotation of solution with addition of Cu(CH$_3$COO)$_2$ and HCl
−0.51	−0.50	–	–
−0.68	−0.75	−0.82	−0.85
−0.6	−0.58	–	–
−0.58	–	–	–
−0.53	–	–	–
−0.72	–	–	–
−0.56	–	–	–

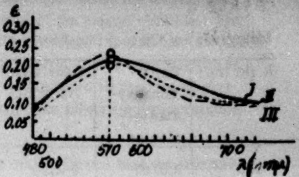


Fig. 1. Optical density of solutions of copper biuret complexes of tripeptides (M. / 300). 1) l-Alanyl-d-alanyl-l-alanine; II) l-alanyl-l-alanyl-l-alanine; III) racemic dialanylalanine.

TABLE 2

Magnitudes of Optical Densities ε of Copper Biuret Complexes of Tripeptides (Tripeptide Concentration M. / 150)

λ (in mμ)	Racemic alanylalanyl-alanine	l-Alanyl-l-alanyl-l-alanine	l-Alanyl-d-alanyl-l-alanine
480	0.0642	0.0630	0.0807
500	0.1202	0.1138	0.1263
520	0.1746	0.1494	0.1601
540	0.2189	0.1752	0.1909
550	0.2251	0.1861	0.2075
560	0.2290	0.1984	0.2156
570	0.2346	0.2170	0.2249
580	0.2180	0.2005	0.2150
590	0.2042	0.1990	0.2071
600	0.1822	0.1895	0.2008
620	0.1608	0.1751	0.1910
640	0.1469	0.1523	0.1731
660	0.1256	0.1342	0.1587
680	0.1172	0.1258	0.1377
700	0.1091	0.1184	0.1241
730	0.1065	0.1021	0.1104

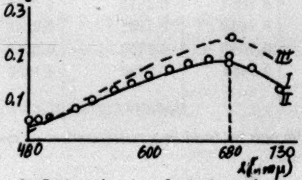
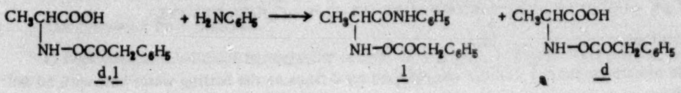


Fig. 2. Optical density of solutions of copper biuret complexes of dipeptides (M. / 150). I) Racemic alanylalanine; II) l-alanyl-l-alanine; III) d-alanyl-l-alanine.

of the spectrum by biuret complexes does not depend on the optical activity of the substance. It is also particularly interesting to note that similar absorptions are exhibited not only be racemic and optically active alanyl peptides but also by the complex of the alanyl tripeptide whose amino acids do not all possess the same type of rotation (l-alanyl-d-alanyl-l-alanine). Not less important is the observation that the absorption by complexes of alanyl peptides is nearly identical with the absorption of the corresponding glycyl di- and tripeptides.

EXPERIMENTAL

Optically active forms of alanine were prepared by resolution of racemic carbobenzoxyalanine with the help of active papaine. The fermentative synthesis of the anilide proceeds only with the natural l-form of alanine in the form of the carbobenzoxy compound), the carbobenzoxy-d-alanine remaining in solution:



$$\underset{\underline{d,l}}{\underset{NH-OCOCH_2C_6H_5}{CH_3CHCOOH}} + H_2NC_6H_5 \longrightarrow \underset{\underline{l}}{\underset{NH-OCOCH_2C_6H_5}{CH_3CHCONHC_6H_5}} + \underset{\underline{d}}{\underset{NH-OCOCH_2C_6H_5}{CH_3CHCOOH}}$$

TABLE 3

Magnitudes of Optical Densities ε of Copper Biuret Complexes of Dipeptides (Concentration of Dipeptide M./150)

λ (in mμ)	Carbobenzoxyalanylalanine	Alanylalanine (racemic)	Carbobenzoxy-l-alanyl-l-alanine	l-Alanyl-l-alanine	Carbobenzoxy-d-alanyl-l-alanine	d-Alanyl-l-alanine
480	0.0107	0.0310	0.0329	0.0489	0.0300	0.0185
500	0.0232	0.0402	0.0413	0.0491	0.0689	0.0421
520	0.0482	0.0799	0.0833	0.0696	0.0970	0.0855
540	0.0555	0.0870	0.0888	0.0930	0.1411	0.1121
560	0.0799	0.1098	0.1234	0.1049	0.1569	0.1270
580	0.1036	0.1160	0.1621	0.1162	0.1772	0.1324
600	0.1412	0.1504	0.2020	0.1506	0.1886	0.1822
620	0.1691	0.1600	0.2055	0.1608	0.2102	0.2050
640	0.1778	0.1705	0.2301	0.1704	0.2111	0.2101
650	0.1891	0.1770	0.2313	0.1760	0.2198	0.2359
660	0.1897	0.1790	0.2356	0.1790	0.1956	0.2442
670	0.1657	0.1810	0.2250	0.1818	0.1957	0.2485
680	0.1644	0.1851	0.2248	0.1886	0.1937	0.2377
700	0.1541	0.1720	0.2219	0.1732	0.1859	0.2025
730	0.1433	0.1350	0.1452	0.1304	0.1504	0.1933

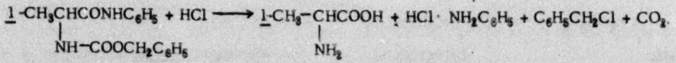
Use was made of Bergman's method of resolution[4], which he proposed for the resolution of carbobenzoxy-d,l-leucine.

Preparation of the anilide of carbobenzoxy-l-alanine. 5 g carbobenzoxyalanine was dissolved in 25 ml 1 N NaOH, and addition was made of 45 ml 2 N sodium acetate, 75 ml citrate buffer, 50 ml papaine solution, 0.075 g freshly reduced cysteine hydrochloride, 5 g freshly distilled aniline and 1 ml glacial acetic acid. A transparent, faint yellow solution was obtained which was stood in a thermostat at 37°. After several hours flocs of the anilide appeared in the vessel, and after 2 days the amount was 2.3 g. The filtrate from the anilide was acidified with 5 N HCl until acid to Congo and extracted with ether. The ether solution was washed with water several times to remove the hydrochloric acid and dried overnight over sodium sulfate, after which the ether was distilled. Yield 3 g with m.p. 90-100°. Resolution evidently did not proceed to completion.

3 g of this substance was dissolved in 15 ml 1 N NaOH, and addition was made of 45 ml citrate buffer, 30 ml papaine solution, 0.045 g reduced cysteine and 3 g freshly distilled aniline. After standing for a day in the thermostat, another 0.5 g anilide came down. The precipitate was filtered and the solution again stood in the thermostat. After 24 hours, another 0.4 g anilide was obtained, making a total of 3.2 g of the anilide of the l-form from 5 g carbobenzoxyalanine. The theoretical yield was 3.3 g. The anilide was purified by recrystallization from alcohol. M.p. 159-160°.

Found %: N 9.23. $C_{17}H_{18}O_3N_2$. Calculated %: N 9.05. Specific rotation of a 6.25% solution in methyl acetoacetate: $[\alpha]_D^{20} = \frac{-0.8 \cdot 100}{6.24 \cdot 1} = -12.8°$.

Hydrolysis of the anilide of carbobenzoxy-l-alanine. The literature does not contain any reference to the separation of the l-form by this method. For this purpose we carried out an acid hydrolysis:



$$\text{l-}\underset{\displaystyle NH-COOCH_2C_6H_5}{CH_3CHCONHC_6H_5} + HCl \longrightarrow \text{l-}\underset{\displaystyle NH_2}{CH_3-CHCOOH} + HCl \cdot NH_2C_6H_5 + C_6H_5CH_2Cl + CO_2.$$

5 g of the anilide of carbobenzoxy-l-alanine was refluxed for 6 hours on the boiling water bath with 50 ml concentrated HCl. Bubbles of gas came off at the start, indicating that hydrolysis of the carbobenzoxy group was proceeding. After 30 minutes the gas ceased to be evolved and the whole of the substance had dissolved in the

acid, the solution acquiring a brown color. The odor of benzyl chloride was detected. After hydrolysis, the solution was cooled and extracted twice with equal volumes of ether for removal of the benzyl chloride. The color of the solution then became lighter. The aqueous layer was evaporated in vacuum, the obtained substance was dissolved in the minimum amount of water and the solution was neutralized with 10% sodium carbonate solution. The aniline was then extracted with benzene and the solution again evaporated in vacuum to give 3.6 g of a yellow substance. The color disappeared after washing with alcohol. The substance was a mixture of sodium chloride and the sodium salt of l-alanine.

The amount of l-alanine salt was determined by formaldehyde titration which showed that the mixture was one-third by weight l-alanine, i.e. 1.2 g. Yield 85.6% of the theoretical.

Preparation of carbobenzoxy-l-alanine was carried out as for racemic alanine.

5 g of the mixture (l-alanine and NaCl), containing 1.5 g l-alanine, was taken. The reaction gave 3.1 g carbobenzoxy-l-alanine or 80.5% of the theoretical. M.p. 84°.

Specific rotation of a 2.5% solution in methyl alcohol: $[\alpha]_D^{20} = \frac{-0.26 \cdot 100}{0.8 \cdot 2.5} = -13°$.

Separation of carbobenzoxy-d-alanine. The mother liquor after removal of the anilide was acidified with 5 N HCl and extracted with ether. The ether layer was washed with water for removal of the HCl and dried with sodium sulfate; the ether was distilled in vacuum.

Yield 2.2 g with m.p. 80-84°. Recrystallization from hot water gave 1.8 g with m.p. 82-84°.

Carbobenzoxy-d-alanine has not previously been prepared. Bergman gives a m.p. of 84° for carbobenzoxy-l-alanine.

The rotation was determined on a 2.5% solution of the substance in methyl alcohol.

$$[\alpha]_D^{20} = \frac{+0.25 \cdot 100}{0.8 \cdot 2.5 \cdot 1} = +12.5°.$$

Carbobenzoxy-d-alanine does not crystallize so readily as racemic carbobenzoxyalanine. Crystallization requires a long period and intense cooling. Other properties are similar.

Synthesis of alanine dipeptides. Bergman's general method was used. Alanine dipeptides have not previously been obtained by this method. The principal difficulties in performing the syntheses were the following:

I. The acid chlorides of the carbobenzoxy-optically active forms of alanine have poor stability. The ethyl ether used as solvent must be well cooled; likewise the petroleum ether used for removing the phosphorus oxychloride.

II. Carbobenzoxyalanylalanine has fairly good solubility in water and organic solvents, and this hinders its purification from phosphoric acid. The latter is removed by dissolving the carbobenzoxy-dipeptide in methyl alcohol, adding 10% sodium carbonate solution until alkaline to litmus, evaporating to dryness in vacuum and working up the residue with absolute methyl alcohol. The sodium phosphate is filtered off. The solution of the carbobenzoxy-dipeptide salt in methyl alcohol is acidified with 20% HCl until acid to litmus and neutral to Congo red, and again evaporated to dryness; the carbobenzoxy-dipeptide was dissolved in methyl alcohol and filtered from the NaCl; the alcohol was distilled off and the carbobenzoxy-dipeptide isolated in the free state.

III. Reduction of carbobenzoxyalanyl dipeptides hardly proceeds in the conditions recommended by Bergman. Good results are obtained by reduction in an aqueous medium: 0.6-0.8 g carbobenzoxyalanine was put into 10 ml water and 1 ml glacial acetic acid. Prior to reduction this mixture was in the form of a suspension; with progressive reduction it gradually changed into a transparent solution. Reduction was effected by passing a stream of hydrogen in presence of palladium catalyst.

The following were prepared:

1) Racemic carbobenzoxyalanylalanine (an oil, very soluble in organic solvents and fairly soluble in water).

2) Carbobenzoxy-l-alanyl-l-alanine (an oil less soluble in water than the racemic carbobenzoxyalanylalanine).

3) Carbobenzoxy-d-alanyl-l-alanine (crystals melting at 120°; slow crystallization; poor solubility in water).

The alanine dipeptides crystallize with great difficulty. Tripeptides were synthesized starting from aqueous solutions of the dipeptides (2.8%) in which the ratio of total to amine nitrogen was determined by an analytical method.

The theoretical ratio of total N to amine N is 2.05. For racemic alanylalanine the value found was 2.2; for l-alanyl-l-alanine 2.08; for d-alanyl-l-alanine 2.3.

Alanine tripeptides were synthesized by Bergman's general method via the carbobenzoxy derivatives. Carbobenzoxy-tripeptides are obtained in the form of an oil with better solubility in water than the carbobenzoxy-dipeptides. Prior to reduction, the phosphoric acid was eliminated by the same method as was described above for carbobenzoxy-dipeptides. Reduction was performed in 9 ml water + 1 ml glacial acetic acid until the solution was completely cleared (1 hr). The catalyst was filtered off and the solution evaporated in vacuum; the last traces of water were distilled off with benzene and the tripeptide was crystallized. Alanine tripeptides are very soluble in water; they form a suspension in absolute methyl alcohol.

TABLE 4

Analysis of Tripeptides

Tripeptides	Nitrogen %		Total N: amine N
	Total	Amine	
Racemic alanylalanylalanine	18.21	5.5	3.27
l-Alanyl-l-alanyl-l-alanine	16.49	5.2	3.15
l-Alanyl-d-alanyl-l-alanine	16.51	5.1	3.23
Calculated for $C_9H_{17}O_4N_3$	18.18	6.07	3.23

Compounds prepared by this route were racemic alanylalanylalanine, m.p. 210° (with decomp.), l-alanyl-l-alanyl-l-alanine, m.p. 280° (with decomp.), and l-alanyl-d-alanyl-l-alanine, m.p. 220° (with decomp.).

SUMMARY

1. Formation of the biuret complex of optically active peptides and proteins does not lead to racemization, thus indicating enolization of the peptide bonds during the biuret reaction and providing evidence of the presence of the enol form of the peptide bonds in the structure of the biuret complex of peptides and protein.

2. Formation of the biuret complex permits maintenance of the optical activity of proteins and peptides when exposed to the prolonged action of caustic alkali.

3. The optical activity of peptides does not exert a specific influence on the character of the absorption of biuret complexes in the visible region of the spectrum.

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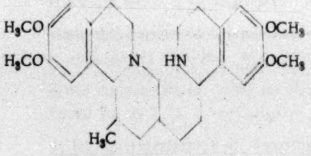
ISOQUINOLINE COMPOUNDS

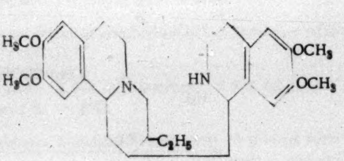
IX. SYNTHESIS OF 1-[δ-(β-METHYL-α-PIPERIDONE)]-2-[1'-(3',4'-DIHYDRO-6',7'-DIMETHOXYISOQUINOLYL)]-ETHANE AND OF THE ETHYL ESTER OF N-HOMOVERATRYL-β-METHYL-α-PIPERIDONE-δ-PROPIONIC ACID

L. I. Zakharkin and N. A. Preobrazhensky

In connection with our studies of the synthesis of compound structurally similar to the alkaloid emetine, we prepared 1-[δ-(β-methyl-α-piperidone)]-2-[1'-(3',4'-dihydro-6',7'-dimethoxyisoquinolyl)]-ethane (I) and the ethyl ester of N-homoveratryl-β-methyl-α-piperidone-δ-propionic acid (II). The synthesis of these compounds revealed the possibility of preparation of a compound with structure (III), possessing one of the formulas previously suggested for emetine.



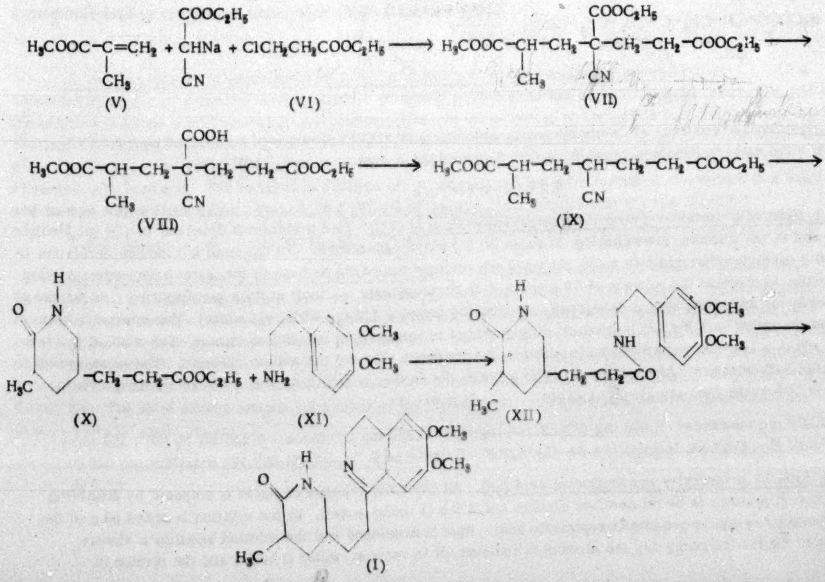
(III)



(IV)

We have previously shown [1], however, that the structure of emetine corresponds to formula (III) and not to formula (IV).

The synthesis described in this paper served as a model for the preparation of compounds required for synthesis of compounds containing the benzoquinolizine grouping. Compound (I) was synthesized according to the following scheme:



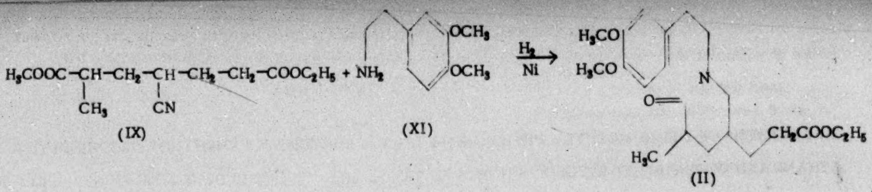
$$H_3COOC-\underset{\underset{CH_3}{|}}{C}=CH_2 + \overset{\overset{COOC_2H_5}{|}}{\underset{\underset{CN}{|}}{C}}HNa + ClCH_2CH_2COOC_2H_5 \longrightarrow H_3COOC-\underset{\underset{CH_3}{|}}{CH}-CH_2-\overset{\overset{COOC_2H_5}{|}}{\underset{\underset{CN}{|}}{C}}-CH_2-CH_2-COOC_2H_5 \longrightarrow$$

(V) (VI) (VII)

$$H_3COOC-\underset{\underset{CH_3}{|}}{CH}-CH_2-\overset{\overset{COOH}{|}}{\underset{\underset{CN}{|}}{C}}-CH_2-CH_2-COOC_2H_5 \longrightarrow H_3COOC-\underset{\underset{CH_3}{|}}{CH}-CH_2-\underset{\underset{CN}{|}}{CH}-CH_2-CH_2-COOC_2H_5 \longrightarrow$$

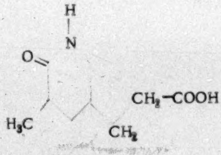
(VIII) (IX)

(X) (XI) (XII) (I)



(IX) (XI) (II)

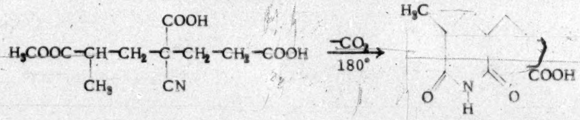
The methyl ester of methacrylic acid (V) condenses [2] with the ethyl ester of sodium cyanoacetate and the product of reaction, without isolation, is worked up with the ethyl ester of β-chloropropionic acid (VI). The resultant ester of α-methyl-γ-cyano-γ-carbethoxypimelic acid (VII) is converted by hydrolysis with one equivalent of alcoholic alkali into the monoacid (VIII), which is transformed by decarboxylation into the ester of α-methyl-γ-cyanopimelic acid (IX). Hydrogenation of the latter gives the derivative of α-piperidone (X), and this is hydrolyzed with one equivalent of alcoholic alkali to the acid (Xa).



(Xa)

Heating of the ester of β-methyl-α-piperidone-δ-propionic acid (X) with homoveratrylamine (XI) gives the corresponding amide (XII), which with phosphorus oxychloride is converted into a crystalline dihydroisoquinoline derivative [4]. If (X) is heated with β-phenylethylamine, a crystalline amide is obtained.

It is interesting to note that hydrolysis of the tricarboxylic ester (VII) with three equivalents of alcoholic alkali gives the tricarboxylic acid (XIII), but on decarboxylation this is converted not into α-methyl-γ-cyanopimelic acid but into the isomeric monobasic acid with the structure (XIV) [3]:



(XIII) (XIV)

Hydrolysis of the ester of α-methyl-γ-cyanopimelic acid (IX) in presence of homoveratrylamine (XI) gives the ethyl ester of N-homoveratryl-β-methyl-α-piperidone-δ-propionic acid [5] (II).

EXPERIMENTAL

1. Ester of α-methyl-γ-cyano-γ-carbethoxypimelic acid (VII). 11.5 g sodium is dissolved in 170 ml absolute alcohol and to the solution, after cooling, is added 56.5 g ethylcyanoacetate. To the resultant sodium derivative is added 50 g methylmethacrylate (b.p. 99-101°) and the mixture heated for an hour on the water bath. After cooling, slow addition is made to the solution of 70 g ethyl β-chloropropionate. Almost at once precipitation commences of sodium chloride and much heat is developed, necesitating periodic cooling with cold water. The solution is then heated on the water bath for two hours until disappearance of the alkaline reaction to litmus. The alcohol is distilled off in a low vacuum and water is added to the residue to dissolve the sodium chloride. The separated oil is extracted with benzene. After removal of the solvent, the residue is distilled. B.p. 197-199° (9 mm). Yield 126.5 g or 81% of the theoretical; n_D^{20} 1.4503.

3.220 mg substance: 6.800 mg CO_2; 2.140 mg H_2O. 5.320 mg substance: 0.216 ml N_2 (23°, 754 mm). Found %: C 57.59; H 7.44; N 4.64. $C_{15}H_{23}O_6N$. Calculated %: C 57.50; H 7.40; N 4.47.

2. Ester of α-methyl-γ-cyanopimelic acid (IX). An alcoholic solution of NaOH is prepared by dissolving 3.7 g sodium (1 g-atom) in 50 ml absolute alcohol and 2.9 g (1 mole) water. To the solution is added 50 g of the ester of α-methyl-γ-cyano-γ-carbethoxypimelic acid. Heat is developed and the solution acquires a viscous consistency. On the following day the alcohol is distilled off in vacuum, water is added and the residue of

alcohol distilled off in vacuum . The unsaponified tricarboxylic ester is extracted with benzene and the aqueous solution (cooled) is acidified with dilute hydrochloric acid. The separated oil is extracted with ether. After drying, the ether is removed and the residue of viscous oil (40 g) is heated for 40 minutes at 170-175° until carbon dioxide ceases to come off. After cooling, the mobile oil is dissolved in 50 ml benzene and the benzene solution washed 2-3 times with 5% NaOH solution for removal of acid impurities. After drying, the solvent is removed and the residue fractionated in vacuum. Yield 22 g (57.2% of the theoretical). B.p. 183-186° at 14 mm; n_D^{20} 1.4431. 5 g unsaponified ester is recovered unchanged.

3.345 mg substance: 7.360 mg CO_2; 2.350 mg H_2O. 5.620 mg substance: 0.298 ml N_2 (25°, 752 mm). Found %: C 60.01; H 7.86; N 6.01. $C_{12}H_{19}O_4N$. Calculated %: C 59.71; H 7.94; N 5.80.

3. Ethyl ester of β-methyl-α-piperidone-δ-propionic acid (X). Into an autoclave is charged 5 g pyrophoric nickel, 20 ml absolute alcohol and 19.2 g of the ester of α-methyl-γ-cyanopimelic acid. Hydrogenation is performed at 105-110° and 150-160 atm for an hour. The alcoholic solution is filtered fromcatalyst and the alcohol removed on the water bath. The residual thick oil is distilled in vacuum. B.p. 163-165° (3 mm). Yield 13.7 g (80.5% of theory), n_D^{20} 1.4830. Colorless, viscous oil.

3.5030 mg substance: 7.9530 mg CO_2; 2.6820 mg H_2O. 4.4480 mg substance: 10.084 mg CO_2; 3.4070 mg H_2O. 5.910 mg substance: 0.345 ml N_2 (22°, 755 mm). Found %: C 61.92, 61.83, H 8.56, 8.57; N 6.71. $C_{11}H_{19}O_3N$. Calculated %: C 61.93; H 8.90; N 6.58.

When this compound is saponified with one equivalent of alcoholic KOH, β-methyl-α-piperidone-δ-propionic acid (Xa) is obtained. M.p. (from alcohol) 159-160°.

4.965 mg substance: 0.335 ml N_2 (21°, 750 mm). 4.945 mg substance: 0.324 ml N_2 (20°, 751 mm). Found %: N 7.73, 7.54. $C_9H_{15}O_3N$. Calculated %: N 7.57.

4. Homoveratrylamide of β-methyl-α-piperidone-δ-propionic acid (XII). 3 g ethyl ester of β-methyl-α-piperidone-δ-propionic acid and 2.6 g homoveratrylamine are heated on an oil bath at 180-185° for 4 hours. After cooling, benzene is added and the mass dissolves when heated. While cooling, a colorless oil separates from the benzene solution. The benzene is decanted off and the product washed with a fresh portion of benzene. Clear, very viscous oil. Yield 4.5 g (79.2 % of the theoretical).

3.740 mg substance: 0.276 ml N_2 (24°, 737 mm). Found %: N 8.22. $C_{19}H_{28}O_4N_2$. Calculated %: N 8.04.

In a similar manner from β-phenylethylamine is obtained the phenylethylamide of β-methyl-α-piperidone-δ-propionic acid in crystalline form. M.p. (from alcohol) 162-163°.

4.051 mg substance: 0.346 ml N_2 (18°, 722 mm). Found %: N 9.52. $C_{17}H_{24}O_2N_2$. Calculated %: N 9.71.

5. 1-[δ-(β-Methyl-α-piperidone)]-2-[1'-(3',4'-dihydro-6',7'-dimethoxyisoquinolyl)]-ethane (I). 1.8 g homoveratrylamide of β-methyl-α-piperidone-δ-propionic acid is dissolved by heating in 30 ml toluene and to the solution is added 4 ml phosphorus oxychloride. The mixture is heated at the gentle boil for an hour. After cooling, the weakly colored toluene solution is decanted from the precipitate. The latter is washed once with ether and dissolved in water. The aqueous solution is made alkaline with ammonia and the resultant oil is extracted with benzene. The benzene is distilled off in vacuum and the solid residue is transferred to a filter and washed with a little ether. Yield 1.05 g (61.5% of theory). M.p. (from benzene) 165.5-166.5°.

5.805 mg substance: 0.438 ml N_2 (25°, 754 mm). Found %: N 8.57. $C_{19}H_{26}O_3N_2$. Calculated %: N 8.48.

6. α-Methyl-γ-cyano-γ-carboxypimelic acid (XIII). An alcoholic solution of NaOH is prepared by dissolving 2.21 g (3 g-atoms) sodium in 50 ml absolute alcohol and 1.72 g (3 moles) water To the solution is added 10 g (1 mole) of the ester of α-methyl-γ-cyano-γ-carboxypimelic acid. Hydrolysis proceeds with considerable heat development and the viscosity increases due to separation of the sodium salt. After heating on the water bath for 4 hours, 50 ml water is added and the alcohol is distilled off in vacuum. The transparent aqueous solution is acidified with dilute hydrochloric acid and extracted with ether. After drying, the ether is driven off. The solid residue weighs 7.2 g (92% of the theoretical). After recrystallization from ether, the m.p. is 169-170° (with decomp.).

4.250 mg substance: 0.224 ml N_2 (23°, 754 mm). Found %: N 6.03. $C_{10}H_{13}O_6N$. Calculated %: N 5.76.

Carbon dioxide was evolved when 7 g α-methyl-γ-cyano-γ-carboxypimelic acid was heated at 170-180°. After cooling, the substance is in the form of a light-brown vitreous mass. Yield 5.7 g.

0.2213 mg substance. Neutralization 9.50 ml 0.1146 N NaOH. Found: M 202. $C_9H_{13}O_4N$. Calculated: M 199.

7. Ethyl ester of N-homoveratryl-β-methyl-α-piperidone-δ-propionic acid (II). 10 g of the ester of α-methyl-γ-cyanopimelic acid was hydrogenated in presence of 20 ml absolute alcohol, 40 g homoveratrylamine and 5 g nickel catalyst at 105-110° and 150-160 atm. for 2 hours. A strong odor of ammonia was detected when the autoclave was opened. The catalyst was filtered off and the alcoholic solution evaporated in vacuum. The residue was dissolved in 100 ml benzene and the benzene solution washed with dilute hydrochloric acid to remove the excess of homoveratrylamine. The benzene was distilled off and the residue fractionated in vacuum. B.p. 225-229° at 1 mm. Yield 3.5 g (22.9% of the theoretical). The compound is a light-yellow, very viscous oil.

3.670 mg substance: 8.965 mg CO_2; 2.615 mg H_2O. 3.220 mg substance: 7.900 mg CO_2; 2.350 mg H_2O. 6.790 mg substance: 0.175 ml N_2 (22°, 745 mm). Found %: C 66.62, 66.90; H 8.16, 8.16; N 3.84. $C_{21}H_{31}O_5N$. Calculated %: C 66.80; H 8.28; N 3.71.

SUMMARY

1. Synthesis was effected through a series of stages of 1-[δ-(β-methyl-α-piperidone)]-2-[1'-(3',4'-dihydro-6',7'-dimethoxyisoquinolyl)]-ethane and of the ethyl ester of N-homoveratryl-β-methyl-α-piperidone-δ-propionic acid, which are the principal intermediate products in model syntheses of emetine.

2. A method is developed for the preparation of the starting materials for these compounds: the ester of α-methyl-γ cyanopimelic acid and the ester of β-methyl-α-piperidone-δ-propionic acid.

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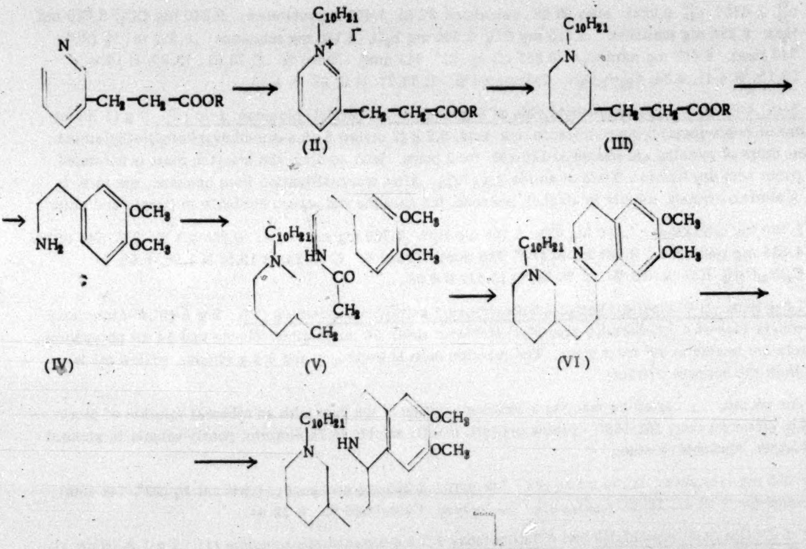
* See Consultants Bureau Translation, p. 1611.

ISOQUINOLINE COMPOUNDS

X. SYNTHESIS OF 1-β-[(N-DECYL)-3'-PIPERIDYL]-ETHYL-6,7-DIMETHOXY-1,2,3,4-TETRAHYDROISOQUINOLINE

R. S. Livshits*, M. S. Bainova, S. D. Kupriyanova and N. A. Preobrazhensky

In view of the valuable physiological action of the alkaloid emetine, it is undoubtedly of interest to prepare simpler compounds containing the fundamentals of its structure. In this manner we may elucidate the influence of the individual structural fragments of the emetine molecule by observing their physiological effects. We effected the synthesis of 1-β-[(N-decyl)-3'-piperidyl]-ethyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (I), a compound whose structure differs from one of the formulas proposed for the natural alkaloid mainly in that the benzoquinolizine ring is substituted by a piperidine ring with an aliphatic radical attached to nitrogen and containing the same number of carbon atoms as in the absent part of the benzoquinolizine ring. The synthesis of compound (I) proceeded according to the following scheme:



(I)

The quaternary salt (II), prepared by condensation of the ester of β-(3-pyridyl)-propionic acid with decyl iodide, is reduced in presence of platinum oxide to the ester of β-[(N-decyl)-3-piperidyl]-propionic acid (III). This ester is heated with excess of homoveratrylamine (IV) at 180-185° to give β-(3',4'-dimethoxyphenyl)-ethylamide-β-[(N-decyl)-3-piperidyl]-propionic acid (V). Under the action of phosphorus oxychloride the amide (V) undergoes cyclization to the isoquinoline derivative (VI). The base (VI) is reduced by zinc and sulfuric acid to 1-β-[(N-decyl)-3'-piperidyl]-ethyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (I). Treatment with an ethereal solution of hydrogen chloride converts it into the hydrochloride.

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* Deceased.

EXPERIMENTAL

Decoiodide of β-(3-pyridyl)-propionic acid ethyl ester (II). 4.4 g (1 mole) of the ethyl ester of β-(3-pyridyl)-propionic acid and 7 g (1.1 moles) decyl iodide are heated at 100-105° and 15-20 mm for 2 hours. The reaction mass — a yellow oil — is washed several times with absolute ether. Yield of quaternary salt 10.2 g (92.5 % of the theoretical). Readily soluble in alcohol and benzene, insoluble in ether and cold water.

8.610 mg substance: 0.227 ml N_2 (18.5°, 747 mm). 8.950 mg substance: 0.249 ml N_2 (19°, 748 mm). Found %: N 3.00, 3.14. $C_{20}H_{34}O_2NI$. Calculated %: N 3.13.

Ethyl ester of β-[(N-decyl)-3-piperidyl]-propionic acid (III). A solution of 10 g decoiodide of β-(3-pyridyl)-propionic acid ethyl ester in 30 mg absolute alcohol and 1 ml glacial acetic acid is hydrogenated at 0.8 atm pressure over 0.3 g platinum oxide. Yield 9.2 g (90.8 % of the theoretical). M.p. 89-90°. The hydroiodide is a colorless, crystalline substance, soluble in alcohol, benzene and chloroform, insoluble in ether and water.

7.900 mg substance: 0.217 ml N_2 (21.5°, 751.5 mm). 7.355 mg substance: 0.202 ml N_2 (1.5°, 751 mm). Found %: N 3.11, 3.10. $C_{20}H_{40}O_2NI$. Calculated %: N 3.09.

A solution of 9 g of the hydroiodide in a little dry chloroform is treated with chloroform saturated with ammonia while cooling. Partial distillation of the chloroform in vacuum and addition of absolute ether led to complete precipitation of the ammonium iodide. Yield 5.76 g (89.2% of theory). The ester is a colorless liquid with b.p. 194-195° at 5 mm, soluble in alcohol, chloroform and benzene, insoluble in water.

n_D^{20} 1.4639; d_{20}^{20} 0.9131; MR_D 98.29, calculated 97.95. 3.460 mg substance: 9.340 mg CO_2; 3.710 mg H_2O. 3.225 mg substance: 8.715 mg CO_2; 3.505 mg H_2O. 8.135 mg substance: 0.322 ml N_2 (20° 745 mm). 6.465 mg substance: 0.252 ml N_2 (21°, 743 mm). Found %: C 73.61, 73.69; H 12.0, 12.15; N 4.41, 4.34. $C_{20}H_{39}O_2N$. Calculated %: C 73.77; H 12.08; N 4.30.

β-(3',4'-Dimethoxyphenyl)-ethylamide of β-[(N-decyl)-3-piperidyl]-propionic acid (V). 2 g (1 mole) ethyl ester of β-[(N-decyl)-3-piperidyl]-propionic acid, 2.2 g (2 moles) β-(3,4-dimethoxyphenyl)-ethylamine and a few drops of pyridine are heated at 180-185° for 2 hours. With cooling, the reaction mass is triturated several times with dry ligroin. Yield of amide 2 g (70%). After recrystallization from benzene, the m.p. is 89-90°. Colorless crystals, soluble in alcohol, benzene, hot gasoline and water; insoluble in ligroin and ether.

2.930 mg substance: 7.870 mg CO_2; 2.755 mg H_2O. 4.720 mg substance: 0.255 ml N_2 (23°, 746 mm). 4.535 mg substance: 0.245 ml N_2 (23°, 746 mm). Found %: C 73.25; H 10.5; N 5.98, 6.02. $C_{28}H_{48}O_3N_2$. Calculated %: C 72.98; H 10.51; N 6.08.

1-β-[(N-decyl)-3'-piperidyl]-ethyl-6,7-dimethoxy-3,4-dihydroisoquinoline (VI). 2 g β-(3',4'-dimethoxyphenyl)-ethylamide of β-[(N-decyl)-3-piperidyl]-propionic acid, 20 ml absolute toluene and 14 ml phosphorus oxychloride are heated at 80° for 2 hours. The reaction mass is worked up and 0.8 g viscous, yellow oil is isolated from the benzene extract.

The picrate is prepared by reacting a benzene solution of the base with an ethereal solution of picric acid. M.p. (from alcohol) 162-163°. Yellow crystals, readily soluble in chloroform, poorly soluble in alcohol and cold water, insoluble in ether.

2.255 mg substance: 0.254 ml N_2 (23°, 742 mm). 2.225 mg substance: 0.247 ml N_2 (23°, 741 mm). Found %: N 12.41, 12.33. $C_{28}H_{46}O_2N_2 \cdot 2C_6H_3O_7N_3$. Calculated %: N 12.44.

1-β-[N-Decyl)-3'-piperidyl]-ethyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (I). 1 g 1-β-[N-decyl)-3'-piperidyl]-ethyl-6,7-dimethoxy-3,4-dihydroisoquinoline was reduced in a medium of 30 ml water, 5 g zinc dust and 3 ml sulfuric acid (sp.gr. 1.84) Yield of reduced base 0.7 g (70 % of the theoretical).

Treatment of a benzene solution of the base with an ethereal solution of HCl gave an oil which crystallized after rubbing. The hydrochloride is a hygroscopic substance, readily soluble in alcohol, chloroform and water, insoluble in ether. M.p. 155-162°, deliquesces at 100-102°.

2.995 mg substance: 7.095 mg CO_2; 2.55 mg H_2O. 7.825 mg substance: 0.385 ml N_2 (22°, 742 mm). 4.240 mg substance: 0.216 ml N_2 (22°, 742 mm). Found %: C 64.61; H 9.53; N 5.46, 5.64. $C_{28}H_{48}O_2N_2 \cdot 2HCl$. Calculated %: C 64.94; H 9.35; N 5.41.

SUMMARY

1. The simplest analog of the alkaloid emetine was synthesized: 1-β-[(N-decyl)-3'-piperidyl]-ethyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline.

2. Methods were developed for the preparation of: the decoiodide of β-(3-pyridyl)-propionic acid ethyl ester; the ethyl ester of β-[(N-decyl)-3-piperidyl]-propionic acid; β-(3',4'-dimethoxyphenyl)-ethylamide of β-[(N-decyl)-3-piperidyl]-propionic acid; and 1-β-[(N-decyl)-3'-piperidyl]-ethyl-6,7-dimethoxy-3,4-dihydroisoquinoline.

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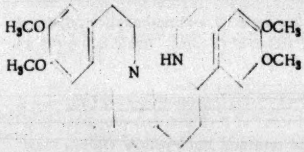
ISOQUINOLINE COMPOUNDS

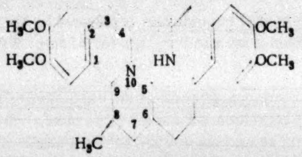
XI. SYNTHESIS OF 1-β-[/N-β-(3",4"-DIMETHOXYPHENYL)-ETHYL/-3'-PIPERIDYL]-ETHYL-6,7-DIMETHOXY-1,2,3,4-TETRAHYDROISOQUINOLINE

R. S. Livshits*, M. S. Bainova, A. I. Gurevich and N. A. Preobrazhensky

With the aim of preparing compounds close to the alkaloid emetine in structure, we effected the synthesis of 1-β-[/N-β-(3",4"-dimethoxyphenyl)-ethyl/-3'-piperidyl]-ethyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (I):


H$_3$CO
H$_3$CO
N
HN
OCH$_3$
OCH$_3$

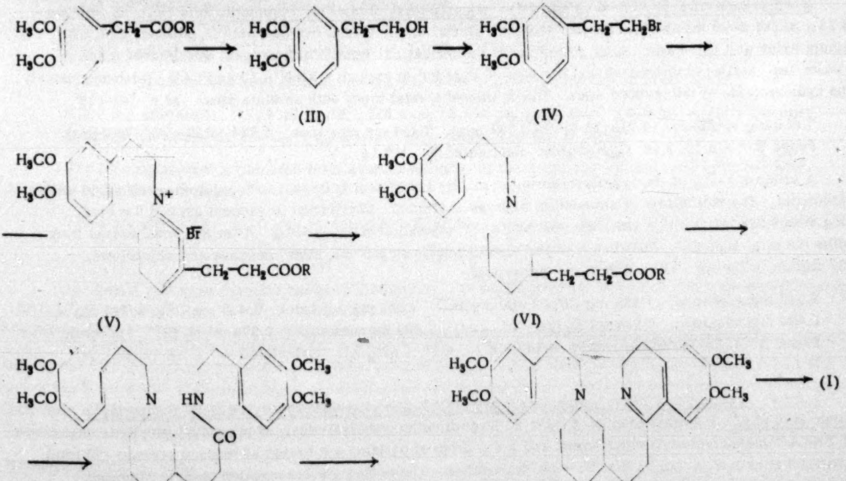
(I)


H$_3$CO
H$_3$CO
3
2
4
1
N
9
10
5
8
7
6
H$_3$C
HN
OCH$_3$
OCH$_3$

(II)

The structure of this substance differs from one of the formulas previously advanced for emetine (II) in that the benzoquinolizine ring is opened at the 1-9 bond and the methyl group in the 8-position is absent.

Compound (I) was synthesized by the following scheme:


H$_3$CO
H$_3$CO
CH$_2$—COOR
H$_3$CO
H$_3$CO
CH$_2$—CH$_2$OH
H$_3$CO
H$_3$CO
CH$_2$—CH$_2$Br
(III)
(IV)
H$_3$CO
H$_3$CO
N+
Br̄
—CH$_2$—CH$_2$COOR
(V)
H$_3$CO
H$_3$CO
N
—CH$_2$—CH$_2$—COOR
(VI)
H$_3$CO
H$_3$CO
N
HN
CO
OCH$_3$
OCH$_3$
(VII)
H$_3$CO
H$_3$CO
N
N
OCH$_3$
OCH$_3$
(I)
(VIII)

---

* Deceased.

Heating of β-(3,4-dimethoxyphenyl)-ethyl bromide (IV) with the ethyl ester of β-(3-pyridyl)-propionic acid gives the corresponding quaternary salt (V), which is transformed by catalytic hydrogenation into the ethyl ester of β-[/ N- β-(3',4'-dimethoxyphenyl)-ethyl/ -3-piperidyl]-propionic acid (VI). By condensation of the latter with β-(3,4-dimethoxyphenyl)-ethylamine we obtain the amide (VII). Treatment of this amide with phosphorus oxychloride gives the dihydroisoquinoline derivative (VIII), which is reduced (zinc dust and sulfuric acid) to 1-β-[/ N-(3",4"-dimethoxyphenyl)-ethyl/ -3'-piperidyl]-ethyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (I). Reaction of the base with picric acid solution gives the picrate. Treatment with HCl solution gives the hydrochloride. Reaction of solutions of the hydrochloride and chloroplatinic acid gives the chloroplatinate.

EXPERIMENTAL

1. β-(3,4-Dimethoxyphenyl)-ethyl alcohol (III) is prepared by the usual method, for example, by reduction with sodium (16.5 g) of the ethyl ester of 3,4-dimethoxyphenylacetic acid (20 g) in a medium of absolute alcohol (100 ml). Yield of crystalline alcohol 8.9 g (54.75 % of the theoretical). B.p. 172-173° (10 mm). M.p. 47-48°

2. β-(3,4-Dimethoxyphenyl)-ethyl bromide (IV) is prepared by heating 5 g β-(3,4-dimethoxyphenyl)-ethyl alcohol with 25 g phosphorus tribromide on a boiling bath for 2 hours. B.p. 153-155° (7 mm). Yield 4.9 g (72.8% of the theoretical).

3. Bromo-β-(3',4'-dimethoxyphenyl)-ethylate of the ethyl ester of β-(3-pyridyl)-propionic acid (V). 4.8 g (1 mole) β-(3,4-dimethoxyphenyl)-ethyl bromide and 4 g (1.14 moles) ethyl ester of β-(3-pyridyl)-propionic acid are heated in vacuum (8-10 mm) on an oil bath at 105-110° for 2 hours. The resultant light-yellow viscous mass is precipitated with absolute ether from the alcoholic solution. Yield after drying in a vacuum desiccator is 8.25 g (99.3 % of the theoretical yield) of quaternary salt; readily soluble in water and alcohol, insoluble in ether.

6.675 mg substance: 0.206 ml N_2 (22°, 758 mm). 6.690 mg substance: 0.201 ml N_2 (22°, 758 mm).
Found %: N 3.49, 3.41. $C_{20}H_{26}O_4NBr$. Calculated %: N 3.30.

4. Ethyl ester of β-[/ N- β-(3',4'-dimethoxyphenyl)-ethyl/ -3-piperidyl]-propionic acid (VI). A solution of 8.25 g of (V) in 25 ml absolute alcohol and 1 ml glacial acetic acid is hydrogenated in presence of 0.3 g platinum oxide at 1.5-1.9 atm. After absorption of the theoretical amount of hydrogen, which takes place in 2-3 hours, the catalyst is filtered off and the alcohol distilled in vacuum. Yield 8.15 g (97.4% of the theoretical) of the hydrobromide of the reduced ester. This is washed several times with absolute ether. M.p. 142-143°.

7.610 mg substance: 0.216 ml N_2 (23°, 748 mm). 7.410 mg substance: 0.211 ml N_2 (23°, 748 mm).
Found %: N 3.16, 3.17. $C_{20}H_{32}O_4NBr$. Calculated %: N 3.25.

A solution of 8 g of the hydrobromide in 40 ml dry chloroform is treated with chloroform saturated with dry ammonia. The precipitate of ammonium bromide is drained. Distillation in vacuum gives 6.0 g base, boiling at 206-208° (2 mm). A colorless, viscous liquid, crystallizing on standing. After recrystallization from gasoline the m.p. is 85-86°. Colorless crystals, readily soluble in alcohol, ether, benzene and chloroform, poorly soluble in ligroin. Yield 92% of the theoretical.

3.115 mg substance: 7.830 mg CO_2; 2.480 mg H_2O. 3.355 mg substance: 8.440 mg CO_2; 2.740 mg H_2O.
6.630 mg substance: 0.244 ml N_2 (20°, 741 mm). 7.400 mg substance: 0.274 ml N_2 (21°, 743 mm).
Found %: C 68.54, 68.60; H 8.91, 9.14; N 4.10, 4.12. $C_{20}H_{31}O_4N$. Calculated %: C 68.72; H 8.94; N 4.01.

5. β-(3",4"-Dimethoxy phenyl)-ethylamide of β-[/ N-β-3',4'-dimethoxyphenyl)-ethyl / -3-piperidyl]-propionic acid (VII). 2 g ethyl ester of β-[/ N-β-(3',4'-dimethoxyphenyl)-ethyl/ -3-piperidyl]-propionic acid, 1.8 g β-(3,4-dimethoxyphenyl)-ethyl amine and a few drops of pyridine are heated at reduced pressure (75 mm) in a nitrogen stream on an oil bath at 250-255° for an hour. The cooled viscous reaction mass is triturated several times with ligroin and then with ether. The mass solidifies after prolonged trituration with ether. Weight 2.4 g amide. After recrystallization from gasoline, it forms colorless needles, soluble in alcohol, chloroform and benzene, poorly soluble in ether and ligroin; m.p. 91°. Yield 86 % of the theoretical.

6.155 mg substance: 0.324 ml N_2 (20°, 751 mm). 4.930 mg substance: 0.264 ml N_2 (22°, 747 mm).
Found %: N 5.97, 5.99. $C_{28}H_{40}O_5N_2$. Calculated %: N 5.78.

6. 1-β-[/N-β-(3",4"-Dimethoxyphenyl)-ethyl/-3'-piperidyl]-ethyl-6,7-dimethoxy-3,4-dihydroisoquinoline (VIII). 2.2 g of (VII) is dissolved in 22 ml absolute toluene by heating on the boiling water bath. Into the solution, with stirring, is run from a dropping funnel 16 ml phosphorus oxychloride and the heating is continued for another 2 hours. On cooling, the reaction mass is poured on to ice. The aqueous and toluene layers are decanted and the residue, in the form of a viscous, dark-brown oil, is dissolved in hot water. The cooled aqueous solution is agitated with ether and then treated with sodium carbonate. The base which separates is extracted with benzene. Drying and vacuum distillation of the solvent leaves 1.16 g (54.5% of the theoretical yield) of a viscous, yellow oil.

Reaction of the benzene solution of the base with an ethereal solution of picric acid gives the brick-red picrate. After recrystallization from 50% alcohol, it melts at 97-98° and decomposes at 180°.

3.190 mg substance: 0.292 ml N_2 (22°, 745 mm). 3.460 mg substance: 0.318 ml N_2 (23°, 745 mm). Found %: N 10.18, 10.20. $C_{28}H_{38}O_4N_2 \cdot C_6H_3O_7N_3$. Calculated %: N 10.06.

The hydrochloride is prepared by the action of an ethereal solution of HCl on a chloroform solution of the base. Very hygroscopic, cream-colored compound. M.p. 117-120°.

5.135 mg substance: 0.230 ml N_2 (25°, 747 mm). Found %: N 4.92. $C_{28}H_{38}O_4N_2 \cdot 2HCl$. Calculated %: N 5.19.

7. 1-β-[/N-β-(3",4"-Dimethoxyphenyl)-ethyl/-3'-piperidyl]-ethyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (I). To a mixture of a solution of 1.5 g of the hydrochloride of 1-β-[/N-β-(3",4"-dimethoxyphenyl)-ethyl/-3'-piperidyl]-ethyl-6,7-dimethoxy-3,4-dihydroisoquinoline in 60 ml water and 10 g zinc dust (previously washed with dilute hydrochloric acid and alcohol) is added, with stirring and heating on the boiling water bath, 8 ml sulfuric acid (sp.gr. 1.84) in the course of 1½ hours, after which the heating is continued for an hour. 1.15 g of the reduced base is separated in the usual manner in the form of a light-yellow oil. Yield 90% of the theoretical.

Reaction of ethereal solutions of the base and HCl gives the hydrochloride. Colorless, hygroscopic compound, m.p. 167-180°; deliquesces at 111-113°. Readily soluble in water and alcohol.

2.635 mg substance: 5.970 mg CO_2; 1.970 mg H_2O. 3.125 mg substance: 7.150 mg CO_2; 2.270 mg H_2O. 4.835 mg substance: 0.216 ml N_2 (22°, 741 mm). Found %: C 61.80, 62.40; H 8.36, 8.10; N 4.96. $C_{28}H_{40}O_4N_2 \cdot 2HCl$. Calculated %: C 62.07; H 7.82; N 5.17.

After recrystallization from alcohol, the picrate melts at 104-105° and decomposes at 175°.

3.300 mg substance: 0.299 ml N_2 (22°, 745 mm). 3.150 mg substance: 0.289 ml N_2 (22°, 745 mm). Found %: N 10.11, 10.24. $C_{28}H_{40}O_4N_2 \cdot C_6H_3O_7N_3$. Calculated %: N 10.03.

The chloroplatinate is prepared from aqueous solutions of the hydrochloride and chloroplatinic acid. It is dried at 115° for analysis.

7.943 mg substance: 1.775 mg Pt. Found %: Pt 22.34. $C_{28}H_{40}O_4N_2 \cdot H_2PtCl_6$. Calculated %: Pt 22.2.

SUMMARY

1. A new analog of emetine has been synthesized: 1-β-[/N-β-(3",4"-dimethoxyphenyl)-ethyl/-3'-piperidyl]-ethyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline.

2. Methods were developed for the preparation of: bromo-β-(3',4'-dimethoxyphenyl)-ethylate of the ethyl ester of β-(3-pyridyl)-propionic acid; ethyl ester of β-[/N-β-(3',4'-dimethoxyphenyl)-ethyl/-3-piperidyl]-propionic acid; β-(3",4"-dimethoxyphenyl)-ethylamide of β-[/N-β-(3',4'-dimethoxyphenyl)-ethyl/-3-piperidyl]-propionic acid; and 1-β-[/N-β-(3",4"-dimethoxyphenyl)-ethyl/-3'-piperidyl]-ethyl-6,7-dimethoxy-3,4-dihydroisoquinoline.

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VLADIMIR YAKOVLEVICH KURBATOV
AND HIS PHYSICO-CHEMICAL INVESTIGATIONS

(on his 75th Birthday)

V. V. Razumovsky

Professor Vladimir Yakovlevich Kurbatov is one of the oldest of the physical chemists, a student of D. I. Mendeleev and D. P. Konovalov. For 45 years V. Ya. has headed the Chair of Physical Chemistry in the Leningrad Technological Institute; he is its originator. The successful and very fruitful creative duties of V. Ya. Kurbatov have extended for a half century in the field of physical chemistry, continuing and developing the scientific aims of his great teachers. Blazing new trails in the study of the properties and internal structures of liquids, colloids, and gels, V. Ya. enriched his native chemical science with many extensive generalizations and discoveries.

V. Ya. Kurbatov was born on January 24, 1878 in St. Petersburg into a servant's family. In 1896, on finishing the primary government school and the 7th St. Petersburg Gymnasium, he entered the Natural Science Division of the Physico-Mathematical Faculty of St. Petersburg University. In 1897, Vladimir Yakovlevich began to conduct scientific investigations in D. P. Konovalov's laboratory. In 1900 he finished at the St. Petersburg University, and was allowed to remain for preparation for professorship. He very often met D. I. Mendeleev in D. P. Konovalov's laboratory, whose assistant V. Ya. Kurbatov was from 1900-1907, and he often discussed problems in chemical science and the results of his own experimental investigations with him at gatherings.

In 1905, V. Ya. began to teach the course in general chemistry for the St. Petersburg Agronomic Courses, where he also organized the first chemical laboratory. The summer of that year he worked in Henri Le Chatelier's laboratory in Paris. In this laboratory he discovered reagents which made possible the correct differentiation of the constituents of quenched steels.

In 1907, V. Ya. Kurbatov was invited to teach the first complete course in physical chemistry at the St. Petersburg Technological Institute, in which he created the Chair of Physical Chemistry. In 1908 he participated in the organization of the chemical faculty of the Womens' Polytechnical Institute, begun by P. N. Ariyan, and from 1908 to 1923, he taught the course in Physical Chemistry for the future first Russian women engineers.

In 1913, V. Ya. was a member of the commission and main consultant for the construction of a cyanamide plant. Later, it must be mentioned that other factories, in particular potassium hydroxide factories, were constructed with his consultation. In 1915, V. Ya. headed the materials testing laboratory for the Ministry of Agriculture, in which he conducted a series of investigations on the preparation of flexible cast iron, cementation of steel, while studying materials and steels for agricultural implements and machines.

V. Ya. Kurbatov adopted the Great October Socialistic Revolution completely and without reservation. From the start of the revolution, he was an active participant in the construction of Soviet higher schools, in the construction of a new socialist culture. Even in 1917, he was designated consultant to the Peoples Commissariat for Education of the young Soviet republic. In 1918, a state museum was created by the Soviet government in Moscow on the proposal and plan of V. Ya. Kurbatov. A course in commercial economics was organized at the museum, which was then reorganized into the Institute of Communal Economics.

In 1919, V. Ya. was designated a member of the Soviet of Peoples Economy for the Northern Section. V. Ya. Kurbatov was one of the most important of the chemists and scientists advising the government on questions of the chemization of the country for the Sovnarkam of the USSR. V. Ya. contributed great scientific pedagogic, and organizational effort during the first years of the Soviet Rule to the higher institutions of learning in Leningrad, served as professor of Physical and General Chemistry at the Photochemical, Agronomic, and Pedagogic Institutes. In 1924, he taught a course in physical and colloidal chemistry at the War Economy Academy of the Workers' and Peasants' Red Army. In the following years, he participated actively in the organization of teaching in the Workers' University, served as a member of the Commission on Self Education for LOSPS,* and was the organizer of the Chemical Section of the Leningrad Industrial Academy.

During the years of the Stalin five year plans, V. Ya. Kurbatov directed his activities at the development of chemical industry in our country, to the organization of new chemical plants. He served as a member of scientific counsels and as a consultant to the Scientific Research Institute for Plastics, the All-Union Scientific Institute for Fats, Central Laboratory of the "Red Triangle" Factory, the All-Union Aluminum Magnesium Institute, the Central Accumulative Laboratory. In all of these years, V. Ya. conducted an extremely large amount of consultant work on production in work shops and laboratories of Leningrad plants and factories. Discoveries during industrial and laboratory experiments for the solution of actual industrial problems enabled him to formulate new physico-chemical laws and theories.

In the Great Patriotic War of 1941-1945, V. Ya. conducted a series of important experimental investigations for industry, consulted for many plants and factories, developed technical conditions for the storage of artistic memorials (bronze monuments) during the war and blockade of Leningrad. The work of V. Ya. on the preparation of engineers and scientific staffs of the Naval Forces of the USSR deserves mention.

V. Ya. Kurbatov conducted his great general work from the first days of the Great October Socialist Revolution. From 1917 up to the present time, he gave more than two thousand lectures at plants, factories, at military posts, warships, clubs, hospitals, lecture halls, and Courses of Culture on various sciences and scientific technical themes. V. Ya. Kurbatov was one of the organizers and a member of the presidium of the All-Union Scientific Engineering Technical Society of Chemists in its Leningrad Section (1930-1938), a member of the Educational Council of the Scientific Chemical Technical Press (from 1918-1938), a member of the organization committee for the V. I. Mendeleev Congress (1932), a member of the editorial staff of the Journal "Chemistry and Economy" (1929), a member of the presidium of the Society for the Welfare of the Soviet Union and for the Development of the Aviation and Chemical Industries, Leningrad Region (1927). He did varied and very useful work as a deputy of the Leningrad State Counsel during its session (1930-1938).

During his years as professor, V. Ya. educated several generations of Soviet engineers and technologists, many of whom became builders and inventors of the Soviet chemical industry. Among the students of V. Ya. Kurbatov are heads of scientific research institutes and enterprises of the chemical industry, heads of the chairs of higher institutions, and chief engineers of the great plants.

The Soviet authorities honored highly the many years of the great creative work of the scientist inventor, patriot of the Motherland, by awarding the Order of Lenin, the Red Banner of Labor, the medals "For Victory over Germany", and "For Valiant Effort in the Great National War of 1941-1945", and awarded him the honorary title "one distinguished in science and technology".

I

For 50 years (1902-1952) the scientific efforts of professor V. Ya. Kurbatov were directed at the study of the properties and internal structure of liquids. The first investigation of liquids, "On the Relation of Latent Heat of Evaporation and the Density of the Vapor" [1] was on the determination of the heat capacity, latent heat of evaporation, and the compressibility of aniline hydrochloride vapors. V. Ya. established that dissociation varies to a considerable degree with the temperature, as well as the pressure. This first scientific investigation of V. Ya. Kurbatov was honored in 1903 by the Russian Physical Chemical Society by a small prize in the name of A. M. Butlerov.

In 1902, V. Ya. published, for the first time in the history of chemistry, the determination of the latent heat of evaporation of mercury and its heat capacity [2]. This investigation showed the preferential application of mercury vapor over water vapor in heat engines, and served as the stimulus for the designing of heat electrical centers on the mercury water cycle.

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* Leningrad Oblast Trade-Union Council.

In his work on the determination of the latent heat of evaporation of mercury, and on the study of the heat capacity and the latent heat of evaporation of aniline, V. Ya. overcame many great experimental difficulties, and obtained such accurate results that they were entered into the basic reference books on physico-chemical values.

In 1907, on the basis of the study of heat capacity and heat of evaporation of a large number of different organic liquids, V. Ya. Kurbatov came to the conclusion that "the forces of crystal formation affect the properties of substances in the liquid state" [3]. "If not all, then some properties of the amorphous state are related to the ability of the given substance to form a crystal lattice" [4]. Although the above theoretical conclusions of V. Ya. Kurbatov are now not doubted at all, at that time they were met with sharp objections and furious attacks from the side of the defenders of the outmoded and reactionary factions in science. These theoretical generalizations and experimental investigations of over 30 organic liquids were published by V. Ya. in his first monograph, "On Molecules Formed by Compounds with Similar Groups. The Appearance of Association" (St. Petersburg, 1908).

Up to 1916 V. Ya. Kurbatov had investigated more than 150 liquids [5]. As a result of the many investigations, he first showed that the degree of ionic exchange between their molecules had a great effect upon the properties of liquids. According to Kurbatov's suggestions, particles of liquids are not only attracted to each other as a whole, but even exchange ions to a certain extent:

$$\underset{1}{\overset{+}{H}}\underset{1}{\overline{OH}}+\underset{2}{\overset{+}{H}}\underset{2}{\overline{OH}}\rightleftarrows H_2O\rightleftarrows\underset{1}{\overset{+}{H}}\underset{2}{\overline{OH}}+\underset{2}{\overset{+}{H}}\underset{1}{\overline{OH}}$$

This type of transformation depends, according to V. Ya. Kurbatov, on the ease of transition of molecules from the non-ionic to the ionic state, which is aided by the asymmetry of the surrounding molecules and the molecular interaction.

In view of the great amount of experimental difficulties for the determination of the heat capacity of poor conducter liquids, V. Ya. Kurbatov used intermolecular coupling to study their nature. The calculation of the intermolecular coupling of liquids by means of Kurbatov's equations required a knowledge of the value of the heat capacity of superheated vapors, which was only slightly studied at that time. During experiments on the determination of the heat capacity of superheated vapors for 16 substances, he showed: 1) at constant temperatures, the heat capacity of superheated vapors is equal to half the heat capacity of the liquid; 2) the relation between the heat capacity and temperature for superheated vapors, as well as for liquids, is expressed by a straight line, or curves closely resembling straight lines; 3) the molecular weight of liquids with sufficiently large ionic interchange is equal to the weight of the given mass of liquid, whether it is a drop or an ocean. The last suggestion of V. Ya. Kurbatov was debated for a long time in the scientific literature, but after two generations, it found complete experimental basis and was proven by Langmuir at the International Physico-Chemical Conference in 1936 at Edinburgh.

Yearly increasing the number of investigated liquids and the temperature ranges of the experiments, up to 1927 V. Ya. Kurbatov had determined: 1) the heat capacity of 136 liquids at temperatures from 60-350°; 2) the heat capacities of five liquid metals at wide temperature intervals, Hg (from 35 to 346°), Na (99-304°), K (79-150°), Cd (353-562°), Pb (351-446°); 3) the latent heat of evaporation of 125 liquids, for most cases the determinations were made at temperature intervals of 60° (at pressures from 760-100 mm); 4) heat capacities of vapors of 18 substances at various temperatures within intervals of about 60°; 5) boiling points of 194 liquids at 25-900 mm; 6) surface tension and capillary constants of 36 liquids at 0-300°. All of these experimental results and theoretical generalizations composed V. Ya. Kurbatov's third monograph [6].

The later investigations of V. Ya. Kurbatov and his students were directed at the determination of the heat capacity of 450 organic liquids, and to see the effect of various functional groups on their properties. The main results of the scientific investigations of the last quarter century (1927-1952) were presented by him at the 1st International Congress on Physical Chemistry in Paris, at the meetings of the Mendeleev All-Union Chemical Society. A compilation of these investigation was published in monograph form [7-9].

In all of his published papers on liquids, V. Ya. Kurbatov established important laws of the liquid and gaseous states of substances: 1) linear relationship of the heat capacity of gases (super heated vapors) with the temperature; 2) the similarity between the above temperature coefficient of heat exchange of gases and the coefficient of expansion of gases; 3) the equality of the given temperature coefficient of heat capacity of weakly ionized liquids to 0.0022 and its decrease upon going to liquids of greater ionizability; 4) additivity of the molecular heat capacity of liquids; 5) the equality of the given volume of all liquids at a corresponding temperature. All of these laws enabled V. Ya. Kurbatov to propose a new complete association theory of liquids, which, in relation to the degree of ionization, classifies all liquids into a finely divided series from the least ionic liquid, helium II, to molten metals and salts [10].

Using these equations, V. Ya. calculated the intermolecular association for 50 liquids. The parallelism, shown by him, between the increase in the intermolecular association of liquids and their electroconductivity, dielectric constant, and chemical activity resulted in convincing and thorough verification for the polyionic theory of association, according to which the liquid state is a continuously forming and dissociating crystal.

The experimental data of V. Ya. Kurbatov on the determination of the properties of liquids were published as standards by the Inter-Peoples Bureau of Standards and are widely used in Soviet chemical literature, and in particular, in M. Kh. Karapetyants' book on chemical thermodynamics which earned the Stalin prize in 1951. V. Ya. Kurbatov's representation of water, as well as of substances with latent crystalline structure, is the basis for the study of the structure of water in the paper of O. A. Alekina "General Hydrochemistry," the first national course in hydrochemistry which earned the Stalin prize in 1950.

Theoretical and experimental papers of V. Ya. Kurbatov in the field of physico-chemical properties resulted in the development of methods: 1) for the intensive purification of natural waters from organic substances, iron, and manganese; 2) for the softening of mineralized waters with deionizers; and 3) for the conservation of drinking water.

II

The establishment and development of industry in Leningrad: food, leather, fat, cellulose-paper, and laquer pigment, after the first World and Civil War, made the planned study of colloidal phenomena most important. In the period from 1919 to 1923, V. Ya. Kurbatov investigated, in relation to industrial problems, properties of colloidal solutions and gels. In 1924, on the basis of experimental material obtained, he proposed the crystalline polyamphion theory. This theory holds that colloids and gels, whose external appearance shows the absence of crystallization, can exist only in the presence of a microskeleton of seed crystals within them which develops sufficiently slowly. This proposed theory of Kurbatov is being confirmed by all experimental material from 1924 up to the present time. It must be especially mentioned that Kurbatov's theory speaks of the presence of a seed crystal skeleton within gels or colloidal emulsions, and not of the crystallization of the entire gel. The formation and the preservation of gels and colloids is then determined by the following laws established by V. Ya. Kurbatov: 1) the rate of crystallization decreases with increase in the valency of the ions, decreasing with especial rapidity upon going from bivalent to trivalent ions; 2) the stability of the crystals increases on going from ions of low valency to those of high valency, and especially sharply upon going from bivalent to trivalent ions.

According to the suggestions of V. Ya., each ion is a cation in a sufficiently acidic medium, and an anion in a sufficiently basic one; and in the transition state, an amphion. Amphions carry positive and negative charges simultaneously, and at the equal charge state, as a result of the neutralization of the opposing charges and the separation of water, form one general polyamphion. Upon the appearance of seed crystals in the polyamphion, it changes into a crystallo-polyamphion [10-13, 28]. Kurbatov's crystallo-polyamphionic theory resulted in the successful solution of many industrial problems for the Leningrad industry. In particular, the rapid and successful solution of the production of cellulose and motion picture film, control of emulsions for phototechnique, problems of blending of rubber and textiles for shoes, the problem of the production of water proof cartons for the acetonitrile industry, of the thickening of glycerine, of mass corrosion of aluminum products, etc.

The crystallo-polyamphionic theory was changed and developed for the physico-chemical explanations and the study of the phenomenon of life [14]. The recognition of the presence of amphions and polyamphions in electrolytes, led V. Ya. Kurbatov to the polyionic-galizate theory of electrolytes [15-17]. The polyionic-galizate theory not only states that water hydrolyzed electrolytes, but that the electrolyte dissolved in the water simultaneously "galizates", i.e. ionizes the water. The polyionic galizate theory, in particular, explains the different degrees of ionization (dissociation) for the same electrolyte, determining the various properties. (Thus for example, for an 0.5 N solution of $MgSO_4$ these differences are close to 50%).

For the past few years, V. Ya. Kurbatov and his students have conducted the experimental and theoretical development of the basic proposals of the polyionic-galizate theory of solutions.

III

A large part of the scientific creative effort of V. Ya. Kurbatov was occupied in the continuation of the scientific legacy of D. I. Mendeleev, in the development of his great ideas. "We will continue the studies of D. I. Mendeleev", wrote V. Ya. Kurbatov in 1908, "somewhat further. At the present time, we know of two finite individualisms, the lower limits of smallness, the electrons, the upper limit of greatness, the galaxies". As a scientific materialist and dialectic he believed," There is no reason for thinking that individualisms cannot exist which are composed of galaxies as these are composed of solar systems. It is important also not to think of electrons as limits of fineness. If the whole universe is infinite, then electrons can be subdivided" [18]. He notes the transfer of the individualism of the macrocosmos (star systems) to those of the microcosmos (electrons of a smaller order). V. Ya. Kurbatov [19] predicted the discovery of super galaxies-meta galaxies, the existence of which was shown 22 years after his prediction by Hubble and Shapley (1930).

Other important conclusions from his work (1905-1908) is the recognition of the infinite division of the atom itself. Examining the principle of increase in entropy, V. Ya. Kurbatov stated that the increase in entropy counteracts the opposite process, the formation of particles from atoms. "If we generalize the basic principles of thermodynamics for equilibrium of all conditions, tendency for maximum entropy, then it is comprehensible that all similar violations of equilibrium, all individualisms will tend to repel one another, since the further they are from each other, the least is the disturbance of equilibrium in the given position. Conversely, two opposing disturbances will tend to destroy one another, and therefore, tend to approach each other. The appearance of individualisms", continues V. Ya. Kurbatov, "atoms with a defined period of life, disturbs the general tendency for equilibrium. The reason for this we do not know: we can only say that such an individualism is more stable than the scattered individualisms of a lower order" [20].

Naturally, V. Ya. Kurbatov, as a scientist-materialist, was outstanding in the very beginning of our century against one of the various sects of "physical" idealism, the energitism of W. Ostwald. In connection with Ostwaldian energitism, V. Ya. Kurbatov wrote in 1908, "but after these many years it is clear that the energetistic conception of the world, suitable for the expression of discovered facts using different words, cannot in any way explain the nature of the processes which arise" [21].

In 1908 V. Ya. Kurbatov came to the conclusion that two types of chemical compounds existed [22]. According to V. Ya. Kurbatov, "Certain electrons of the atoms separate readily and electrostatic (electrolytic) bonds are formed between atoms as a result, wherein the number of such electrons corresponds to the denominator of the group in the Mendeleev order [in so far as it is not greater than the ability of the atom to add these electrons (4,5,6, and 7 groups)]" [23].

In the first type of chemical compounds, the atoms are bound with each other by the attraction of opposite electrical charges. In the second type, a substitution of one or more electrons of one atom by atoms and groups of atoms occurs.

V. Ya. Kurbatov pointed out that "it is necessary to recognize the existence of special bonds in order to explain compounds not subject to electrolysis, for example $SnCl_4$, CH_4, etc." [22]. These ideas of V. Ya. Kurbatov were of considerable importance for the development of electronic ideas in chemistry, and in many ways, anticipated the theories of Kossel (1916) and Lewis (1916).

V. Ya. Kurbatov had previously discovered the relation between the electroconductivity of metals and their position in the Mendeleev system. The discovery of this relation showed that the electroconductivity decreases upon going from metals of the lower group of the Mendeleev system to those of the upper. Decrease of electroconductivity of metal with increase in temperature was explained by V. Ya. as resulting from the increase in the disordered movement of the metal ions in proportion to the increase in temperature [24]. The increase in electroconductivity of alloys and their very low temperature coefficients of electroconductivity were explained by him as the effect of the formation of local thermocouples between the different atoms. Although all of these generalizations were published by V. Ya. Kurbatov in 1907-1908, after 1916 they began to be assigned to K. Bendix without any basis. We notice, by the way, that the question of the effect of temperature on the electroconductivity of metals was picked up in the foreign scientific literature only in the thirties.

In 1925-1927, V. Ya. Kurbatov proposed a hyperboloid form for D. I. Mindeleev's periodic system of chemical elements [20-27, 10]. Representing the Mendeleev system in the form of a hyperboloid of rotation, he placed the rare earth elements in the center systems, where two spirals unfold, one toward the lighter elements, the other toward the heavier. Such a form representing the periodic system shows the continually related properties and the interruption of the transition of properties from element to element, naturally distributing the rare earths and the actinides.

The long and fruitful work of V. Ya. Kurbatov on the propagandization of the scientific discoveries and investigations of D. I. Mendeleev by compiling and editing many of the collected papers of the scientific genius must be mentioned. He read the report "General Review of the Scientific Activities of Mendeleev" [25] after Mendeleev's death at the first Mendeleev Congress. In 1925, V. Ya. Kurbatov's monograph, "D. A. Mendeleev's Law," appeared, in which more than 100 properties of chemical elements were compared for the families of the periodic system. A series of generalizations were given in this monograph by V. Ya., which arose from the basic principles of the Mendeleev Law [26].

In V. Ya. Kurbatov's monograph, "The D. I. Mendeleev System of Elements and Classification in Chemistry" [10], presented by the Academician of Science of the USSR on the 100th anniversary of the birth of D. I., are given the materialistic and elemental-dialectic basis of the scientific theoretical views of the great Russian scientist and idealist, and their value for the development of modern chemical science was shown.

In conclusion it must be mentioned that V. Ya. Kurbatov is widely known as an architectural historian, expert on monuments of Russian culture. To his writings belong the great monographs: "St. Petersburg," "Pavlovsk," "Gardens and Parks," "Leningrad," and the brochures: "Detskoe (formerly Tsarskoe) Selo," "Gatchina," "Petergof," "Strelna and Oranienbaum," and a series of pamphlets on the history of Russian architecture and art [29].

Vladimir Yakovlevich Kurbatov's life's path is the path of a leading scientist inventor, the path of a fiery patriot of the Motherland who has given all of his knowledge and strength for the service of the Soviet People.

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THE IRREVERSIBLE-MUTUAL SYSTEM WITH IMMISCIBILITY FROM LITHIUM AND CADMIUM CHLORIDES AND SULFATE

D. S. Lesnykh and A. G. Bergman

The results of the investigation of mutual chloride-sulfate systems show that limited mutual solubility of the components of stable pairs in the molten state is shown preferentially in those systems whose composition includes cations with different structures for the outer electronic layer.

The great majority of the ternary mutual systems, with immiscibility in the molten state, that were studied are composed of cations with outer electronic structures of the inert gas type, as well as those with 18 + 2 electrons in the outer layer.

In order to verify the above view, a series of ternary mutual chloride-sulfate systems, using lithium salts in melts, was studied by means of the visual-polythermic method. Among these are the below-reported irreversible-mutual systems with immiscibility from lithium and cadmium chlorides and sulfates (with the outer electronic layer for the lithium ion of 2, for the cadmium ion, 18 electrons).

Binary Systems

System	Characteristic points on the curve	According to the results of other authors		According to our results	
		(% *)	Melting point	(%)	Melting point
$CdCl_2 \rightarrow CdSO_4$	Eutectic	16.5	542 [1]	15	542
$Li_2SO_4 \rightarrow CdSO_4$	Eutectic	31.5	551 [2]	32	550
	Polymorphic transformation of Li_2SO_4	–	570	–	572
$Li_2Cl_2 \rightarrow Li_2SO_4$	Eutectic	53.5	478 [3]	53	478
	Polymorphic transformation of Li_2SO_4	–	572	–	572
	Single form transformation of LiCl	–	–	–	564
$Li_2Cl_2 \rightarrow CdCl_2$	Continuous series of solid solutions with a minimum	77-78	500 [4]	77-78	500
	Single form transformation of LiCl	–	–	–	564

* Equimolecular per cents of the component added.

But immiscibility in systems containing cations with similar outer electronic layers is also possible if the cations and anions (upon interhalogen exchange) are distributed at great distances from each other in the subgroups of the periodic system of D. I. Mendeleev.

Diagonal Cross Sections

The thermal effect of the reaction $Li_2Cl_2 + CdSO_4 \rightarrow CdCl_2 + Li_2SO_4$ is equal to 7.99 kcal per equivalent.

The stable cross section $CdCl_2$-Li_2SO_4 is a binary system with a eutectic at 543° and 3.5% of lithium sulfate. A polymorphic transformation of the latter corresponds to 572°. Immiscibility occurs in the interval of from 8 to 80% of lithium sulfate of 650°. The fusion curve in the above interval is intersected by a straight line situated parallel to the composition axis, as a result of the three phase monoeutectic process. The critical point of the binodal curve was not determined because of the volatilization of cadmium chloride.

The fusion diagram of the unstable cross section Li_2Cl_2-$CdSO_4$ consists of six branches: α, β-lithium chlorides; β, α, β-lithium sulfates and cadmium sulfate, intersecting at 563°, and 10%, 490° and 27.5%, 572° and 39%,

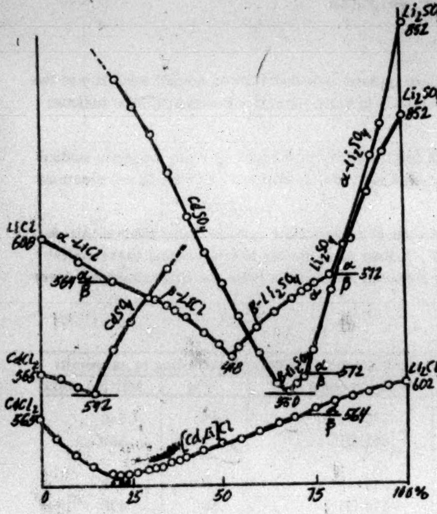

Fig. 1. Lateral sides of the square of the mutual system.

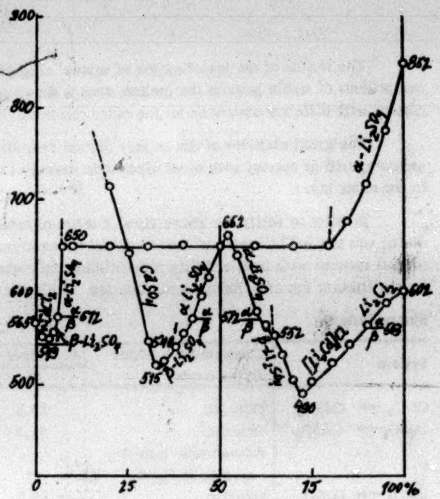

Fig. 2. Diagonal cross sections.

572° and 55.6%, 515° and 67% of cadmium sulfate, respectively. Immiscibility occurs in the melt at 35% of cadmium sulfate at 552° to 62% at 540°. The fusion curve has a maximum at 662°, not at the point of intersection with the stable diagonal, but at 47.5% of cadmium sulfate.

The Mutual System

The surface of the initially separated crystals of the mutual system was investigated with the aid of ten internal sections, the directions of which are shown on Fig. 3; a short characterization of each of these is given in the Composite Table, and on Figs. 4 and 5.

The temperature maximums of all sections, passing through the stable diagonal cross sections in the region of immiscibility, are displaced, in relation to the latter, in the direction of lithium chloride (on Fig. 4 and 5 the stable diagonal is represented by the vertical segments).

The results of the experimental data are generalized in the form of projections of isotherms on the composition square of the mutual system (Fig. 6).

The position of the invariant points, the co-crystallization curve for the components, and curves limiting the region of immiscibility, are presented in the form of projections of the above points and lines of the ternary system $CdCl_2-Li_2SO_4-Li_2Cl_2$ on the side $CdCl_2-Li_2Cl_2$ (Fig. 7), and of the ternary system $CdCl_2-Li_2SO_4-CdSO_4$ on the side $CdSO_4-CdCl_2$ (Fig. 8).

The three phased monoeutectic equilibrium (ab, Figs. 7 and 8) and the polymorphic transformation of lithium sulfate (dotted line) are also described on the projections.

As is apparent (Fig. 6), the mutual system consists of six crystallization poles: cadmium sulfate, occupying 23.4%; α,β-lithium sulfate, 59.3 %; α,β-solid solutions (Li, Cd) Cl, 17.0%, and cadmium chloride, 0.3%, of the total area of the composition square.

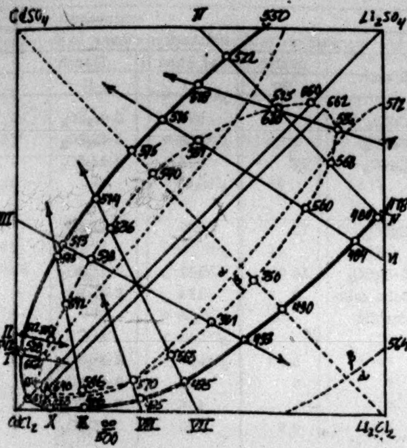
CdSO₄
Li₂SO₄
CdCl₂
Li₂Cl₂
IV
530
572
564
418
III
II
I
X
IX
VIII
VII
VI
V

Fig. 3. Directions of the internal sections

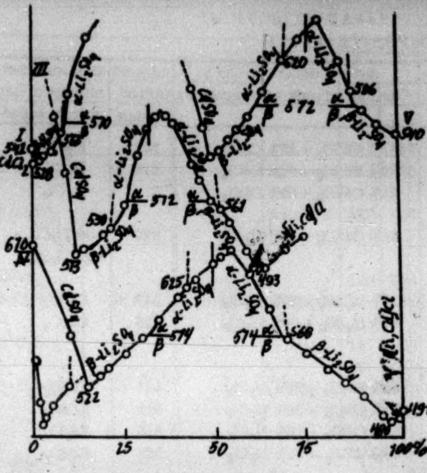

Fig. 4. Internal sections I-V.

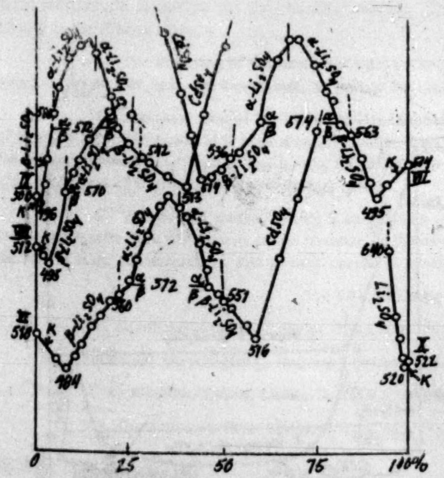

Fig. 5. Internal sections VI-X.

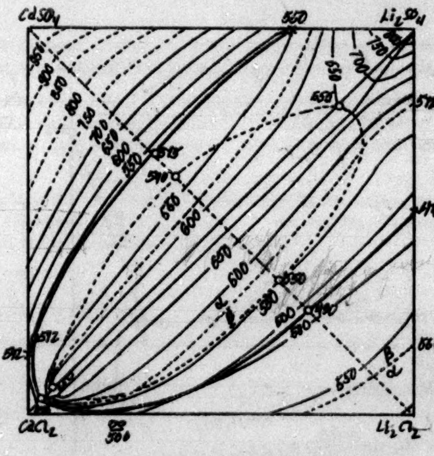
CdSO₄
Li₂SO₄
CdCl₂
Li₂Cl₂
550
572
418
564
512
650
600
700
750
β
α

Fig. 6. Projection of the isotherms on the composition square.

The region of the immiscibility occupies 29.3% of the area of the square.

The stable diagonal cross section $CdCl_2-Li_2SO_4$ divides the square of the mutual system into two ternary systems: $CdCl_2-Li_2SO_4-Li_2Cl_2$ containing the solid solutions (Li, Cd)Cl and the lithium sulfate crystallization pole $CdCl_2-Li_2SO_4-CdSO_4$ with the ternary eutectic, melting at 512°.

COMPOSITE TABLE

Section No.	Initial mixture of components	M.p. of initial mixture	Component or mixture of components added	Branches of the crystallization curves			
				Branch	Intersection of I and II		Branch II
					%*	t°	
I	15% $CdSO_4$ + 85% $CdCl_2$	542	Li_2Cl_2	$CdCl_2$	1	528	β-Li_2SO_4
II	20% $CdSO_4$ + 80% $CdCl_2$	592	Li_2Cl_2	$CdSO_4$	2	512	β-Li_2SO_4
III	50% $CdSO_4$ + 50% $CdCl_2$		Li_2Cl_2	$CdSO_4$	12	513	β-Li_2SO_4
IV	50% $CdSO_4$ + 50% Li_2SO_4	670	50% Li_2Cl_2 + 50% Li_2SO_4	$CdSO_4$	15	522	β-Li_2SO_4
V	70% Li_2SO_4 + 30% Li_2Cl_2	540	$CdSO_4$	β-Li_2SO_4	10	572	α-Li_2SO_4
VI	40% Li_2SO_4 + 60% Li_2Cl_2	518	$CdSO_4$	Solid solution [Li, Cd]Cl	8	484	β-Li_2SO_4
VII	50% $CdCl_2$ + 50% Li_2Cl_2	534	$CdSO_4$	"	8.5	495	β-Li_2SO_4
VIII	65% $CdCl_2$ + 35% Li_2Cl_2	512	$CdSO_4$	"	3	495	β-Li_2SO_4
IX	80% $CdCl_2$ + 20% Li_2Cl_2	500	$CdSO_4$	"	1	496	β-Li_2SO_4
X	90% $CdCl_2$ + 10% Li_2Cl_2	522	$CdSO_4$	"	0.5	520	Li_2SO_4

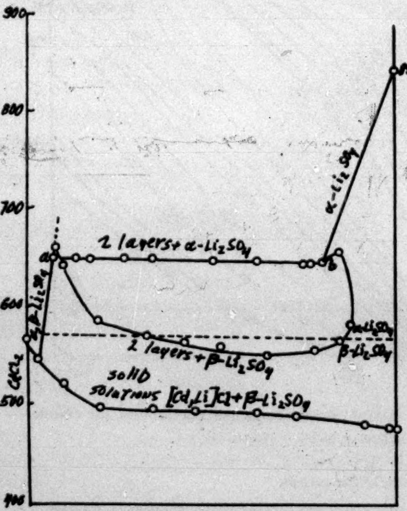

Fig. 7. Projection of the ternary system $CdCl_2-Li_2SO_4-Li_2Cl_2$ on the side $CdCl_2-Li_2Cl_2$.

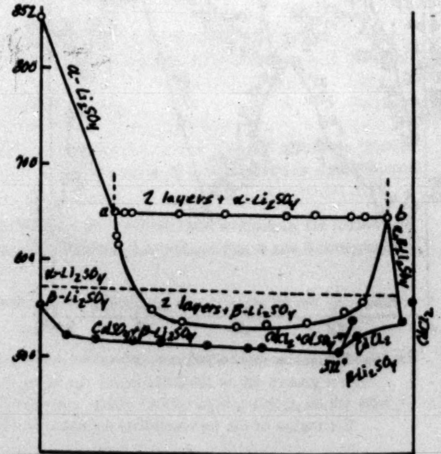

Fig. 8. Projection of the ternary system $CdCl_2-Li_2SO_4-CdSO_4$ on the side $CdSO_4-CdCl_2$.

COMPOSITE TABLE

and their intersections									Immiscibility				Fig. No.
Intersection of I and II		Branch	Intersection of III and IV		Branch	Intersection of IV and V		Branch	From		To		
%	t°	III	%	t°	IV	%	t°	V	%	t°	%	t°	
9	570	α-Li_2SO_4							8	563			4
									10	550			4
27	572	α-Li_2SO_4	50	572	β-Li_2SO_4	62.5	493	Solid sol. [Li,Cd]Cl	22	538	52.5	561	4
31	574	α-Li_2SO_4	68	574	β-Li_2SO_4	98	480	Branch II [Li,Cd]Cl	42.5	625	70	568	4
37	572	β-Li_2SO_4	50	518	$CdSO_4$				12.5	586	30	620	4
24.5	572	α-Li_2SO_4	46	572	β-Li_2SO_4	58.5	516	$CdSO_4$	22	560	50	551	5
18	574	α-Li_2SO_4	40	574	β-Li_2SO_4	55	514	$CdSO_4$	15	563	47	536	5
8	570	α-Li_2SO_4							8	570			5
4.5	572	α-Li_2SO_4	22	574	β-Li_2SO_4	40	513	$CdSO_4$	5	586	28	542	5
									5	640			5

SUMMARY

1. The ternary mutual system of lithium and cadmium chlorides and sulfates was investigated in melts by the visual-polythermic method of physico-chemical analysis. The system is assigned to the irreversible-mutual type with immiscibility in the molten state.

2. The directing of the exchange reaction toward cadmium chloride and lithium sulfate agrees with the thermal effect, equal to 7.99 kcal. per equivalent, as well as the limited mutual solubility of the above layers in the molten state.

3. The large axis of the immiscibility lens coincides with a conoid representing the temperature in the region of immiscibility. This conoid is almost parallel to the stable diagonal cross section, displaced by $\sim$2.5% from the latter in the ternary system $CdCl_2$–Li_2SO_4–Li_2Cl_2. For this reason the immiscibility lens relative to the stable diagonal is asymmetric, and a great part of it affects the above ternary system.

4. The studied mutual system is an example upholding the suggestion that immiscibility in the molten state in most cases results from differences in the structure of the outer electronic layers of the ions, and the resulting difference in the polarization characteristics and physico-chemical properties of the components of the stable pair.

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INVESTIGATION OF COMPLEX FORMATION IN SOLUTIONS OF TERNARY SYSTEMS BY CRYOSCOPIC METHODS

II. SYSTEM $AlBr_3–(C_2H_5)_2O–C_6H_6$

E. Ya. Gorenbein, V. L. Pivnutel, and I. A. Gerasun

The study of the complex compounds of the aluminum halides is of great interest for the clarification of the nature of solutions, as a considerable number of these complex compounds are electrolytes for solvents with small dielectric constants.

The etherates of aluminum halides are examples of these complex compounds.

According to thermal analysis data, aluminum bromide forms a compound of the composition $AlBr_3 \cdot (C_2H_5)_2O$ [1] with ethyl ether. This compound was also obtained in a preparative fashion [2]. Naturally, it was of interest to determine whether or not the composition of this compound would be kept in solution. For this purpose, the viscosity, electroconductivity, density, and the cryoscopy of the given compound were studied in the complete interval of concentration of aluminum bromide and ethyl ether in benzene as the solvent.

Aluminum and other metallic halides form complex compounds which are good electrolytes. The compositions of these electrolytes were mainly determined by means of thermal analysis. Whether or not these electrolytes keep their structures in solution, is difficult to determine, since the majority of these metallic halides is insoluble in low dielectric constant solvents in the absence of aluminum halides.

The composition of the complexes formed by the reaction of aluminum bromide with ethyl ether is readily established in solution, since both components are separately soluble in benzene. For the establishment of the composition of the complex in solution, isomolar concentrations were prepared according to the method reported previously [3].

In the present communication are reported the results of the cryoscopic investigation of two isomolar concentrations of aluminum bromide and ethyl ether in benzene as the solvent, the total moles of which [$AlBr_3$ and $(C_2H_5)_2O$] were equal to 0.05 and 0.15 per mole of benzene.

Starting Materials and Procedure

The benzene was dried and redistilled over metallic sodium after being carefully purified of thiophene. The preparation obtained was stored in sealed ampoules. The ethyl ether, after purification and drying over metallic sodium, was distilled and stored in the same way as the benzene. Aluminum bromide was synthesized by the action of bromine on aluminum shavings according to a method reported previously [4]. The solutions were prepared in a cone-shaped vessel with a side tube and ground glass stopper. Molten aluminum bromide was placed initially into the vessel; after cooling, benzene was weighed and introduced; the desired quantity of ethyl ether was then added to the solution obtained; and finally, the calculated quantity of benzene necessary for the preparation of the desired concentration was added with the aid of a buret. The amount of benzene added was controlled by weight.

It must be mentioned that upon the addition of the ether to the $AlBr_3$ solution in benzene, a considerable heat effect is observed, which shows the presence of an intense reaction between the components of the system. The color of the solution changes in relation to the molecular ratio of the components. With excess $AlBr_3$, the solution is straw yellow, but it becomes almost colorless upon going to an equimolecular ratio of ether to aluminum bromide.

The measurements were conducted in a Beckmann apparatus. The solution was mixed with a nickel stirrer which was actuated by an electromagnet connected with an interrupter. The necessary steps for the protection from traces of moisture were taken during the process.

Results

Solutions were prepared for each isomolar concentration. The freezing point depression was determined not less than three times for each experiment, and the average value was taken. The results of the measurements are given in Tables 1 and 2, and are presented graphically.

In order to trace the extent the molecular composition of the complex formed changes in solution with changes in its concentration, measurements were made with two isomolar concentrations. Although these concentrations were not sufficiently large for cryoscopic investigation, nevertheless the data obtained gave a basis for judging the change of the molecular weight in relation to the concentration of the complex formed in the solution.

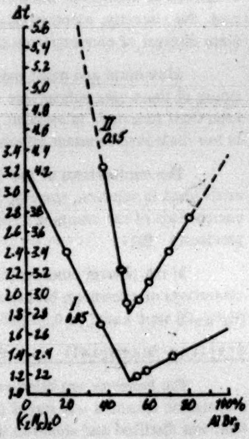
TABLE 1
Cryoscopic Investigation at a Molecular Ratio: $\frac{AlBr_3 + (C_2H_5)_2O}{C_6H_6} = 0.05$

$\frac{AlBr_3 + (C_2H_5)_2O}{C_6H_6}$	Mole % $AlBr_3$	Weight of $AlBr_3$ (g)	Weight of $(C_2H_5)_2O$ (g)	Weight of C_6H_6 (g)	Depression in freezing point of the solution Δt
0.0500	100	–	–	–	1.63*
0.0505	72.32	2.1736	0.2334	17.3173	1.37
0.0498	57.68	2.0180	0.4148	20.3737	1.23
0.0503	53.68	2.8988	0.7009	31.4772	1.19
0.0500	35.71	1.8718	0.9407	30.6464	1.70
0.0490	19.79	1.5810	1.7726	46.5712	2.40
0.0498	0	–	1.1580	24.4311	3.19

At an isomolar concentration equal to 0.15, the depression in freezing point of the binary systems $AlBr_3$–C_6H_6 and $(C_2H_5)_2O$–C_6H_6 could not be measured because of the great depression in temperature and the small scale on the Beckmann thermometer.

TABLE 2
Cryoscopic Investigation at a Molecular Ratio: $\frac{AlBr_3 + (C_2H_5)_2O}{C_6H_6} = 0.15$

$\frac{AlBr_3 + (C_2H_5)_2O}{C_6H_6}$	Mole % $AlBr_3$	Weight of $AlBr_3$ (g)	Weight of $(C_2H_5)_2O$ (g)	Weight of C_6H_6 (g)	Depression in freezing point of the solution Δt
0.1500	80.09	13.3313	0.9254	32.4394	3.73
0.1496	69.10	12.1137	1.5034	34.2799	3.39
0.1499	60.81	10.0782	1.7998	32.3174	3.13
0.1494	55.72	8.5643	1.8920	30.1566	2.95
0.1497	49.46	8.5394	2.4247	33.7619	2.90
0.1493	46.52	8.0373	2.5662	33.8563	3.34
0.1494	44.64	8.2467	2.8429	36.2266	3.61
0.1505	38.75	7.3203	3.2079	36.6937	4.24



Variation of the freezing point with the composition

The figure shows the variation of the depression in freezing point of the solution, Δt, with the mole % of the composition $AlBr_3$ and $(C_2H_5)_2O$, the sum of the moles of which was taken as 100% (the % was calculated from the sum of the moles of $AlBr_3$ and $(C_2H_5)_2O$ without accounting for the solvent). The numerical values of Δt, represented by the inside of the ordinates, correspond to curve II, and were obtained from the data of the isomolar concentration equal to 0.15.

The greatest depression in freezing point of the solution corresponds to the binary systems $AlBr_3$–C_6H_6 and $(C_2H_5)_2O$–C_6H_6. As is seen from the given graph, the smallest depression in freezing point is caused by a 50% (mole) composition of components, which corresponds to the composition of the complex compound formed in the solution, $AlBr_3 \cdot (C_2H_5)_2O$.

It is necessary to mention that the synthesis of this compound by direct reaction of the components [$AlBr_3$ with $(C_2H_5)_2O$] is quite complicated. It is considerably easier to obtain this compound by the above method (i.e., in benzene, and then isolation). For the calculation of the molecular weight of the complex at two concentrations, values for the freezing point depression were taken from the graph at an equimolecular ratio of the components.

Comparison of the molecular states of the complex $AlBr_3 \cdot (C_2H_5)_2O$ in solution at isomolar concentrations of

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* (Calculated theoretically on the basis that the molecular weight of aluminum bromide was double in benzene) [6].

0.05 and 0.15, shows that they correspond to a molecular weight equal to 481.3 and 602.5 respectively.

Therefore, the molecular weight is considerably higher at greater concentrations. The conductivity of these solutions at equimolar concentrations of the components is as follows: at a molecular ratio equal to 0.05, approximately 10^{-6} ohm^{-1}cm^{-1}, and for 0.15, ~ $8 \cdot 10^{-5}$

This is in agreement with the established position that the electroconductivity increases in solvents with small dielectric constants with increase in the degree of association of the electrolyte.

Therefore, it follows from the above results, that a compound of the composition – $AlBr_3 \cdot (C_2H_5)_2O$, is formed in the solution, which can be an electrolyte depending on its concentration, i.e., in the region of higher concentration, it conducts electricity, but on dilution, when the molecular state approaches that of the molecular weight corresponding to the formula $AlBr_3 \cdot (C_2H_5)_2O$, this compound practically stops being a conductor. Such behavior for an electrolyte in solvents of small dielectric constant is in complete agreement with the views of E. Ya. Gorenbein on the nature of concentrated electrolyte solutions [5].

SUMMARY

1. The reaction between $AlBr_3$ and $(C_2H_5)_2O$ in C_6H_6 as the solvent was investigated for two isomolecular concentrations (0.05 and 0.15) by the cryoscopic method.

2. It was shown that a complex compound of the composition $AlBr_3 \cdot (C_2H_5)_2O$ is formed in the solution which is subjected to association with increase in the concentration.

3. It was shown that the complex compound $AlBr_3 \cdot (C_2H_5)_2O$ was an electrolyte at relatively high concentrations in benzene.

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PHYSICO-CHEMICAL INVESTIGATION OF IODINE SOLUTIONS

IX. THE SYSTEMS NICKEL, ZINC, AND CADMIUM IODIDE AMMINES — IODINE IN NITROBENZENE SOLUTIONS

Ya. A. Fialkov and F. D. Shevchenko

As was shown in the previous communications [1,2] nickel iodide hexammine and zinc and cadmium iodide tetrammines form relatively unstable polyiodides in systems with molten iodide, which are found in these systems in associated state and show the properties of fairly strong electrolytes.

For the development of these investigations, it was of great interest to study the reaction of iodine with these ammines in the presence of organic solvents, for which purpose nitrobenzene and aceto nitrile were used.

The following question was posed for the present investigation: Do the polyiodides of nickel, zinc, and cadmium ammines also form in organic solutions, and what is the composition of these polyiodides in the given solution? What are the molecular states and the electrolyte properties of such polyiodides in nitrobenzene and acetonitrile ?

EXPERIMENTAL

The ammines of nickel, zinc, and cadmium iodides were prepared, and the iodine was purified as reported in the previous communications [1, 2]. The nitrobenzene was purified and dried with the usually applied method [3]. B.p. 210.5° and freezing p. 5.5°.

Acetonitrile was distilled, kept for several days over fused calcium chloride, and once more redistilled taking a fraction at 82°. The solvents were kept in sealed test tubes.

Specially planned experiments showed that $Ni(NH_3)_6I_2$, $Cd(NH_3)_4I_2$, and $Zn(NH_3)_4I_2$ were not noticeably soluble in nitrobenzene and acetonitrile, but that they were sufficiently soluble in nitrobenzene and acetonitrile iodine solutions.

An accurately weighed sample of the ammines of nickel, zinc, or cadmium iodide, taken in a quantity greater than the solubility of the ammine in the iodine solution of the given concentration, was added to a predetermined quantity of an iodine solution in nitrobenzene or acetonitrile in a flask with a well-ground-in stopper. The contents of the flask were shaken for 5-6 hours at 20°, then the undissolved ammine was quantitatively transferred on a filter, washed with alcohol and ethyl ether,* dried, and weighed. In this fashion, the amount of the ammine going into solution was determined. The results of these determinations are given in Tables 1 and 2.

The amount of nickel, zinc, and cadmium iodide ammines which dissolves in nitrobenzene and acetonitrile solutions of iodine at 20° increases with the increase of the iodine in the solution. However, the molecular ratio of the iodine in the solution and the ammine dissolved almost does not change even when the concentration of iodine in these solutions is increased by 3-4 times.

The molar ratios of iodine and ammine found in these experiments correspond, generally, to the following polyiodides:

1) In nitrobenzene solutions — $Ni(NH_3)_6I_2 \cdot 3I_2$, $Zn(NH_3)_4I_2 \cdot 2I_2$, $Cd(NH_3)_4I_2 \cdot 2I_2$; 2) in acetonitrile solutions — $Ni(NH_3)_6I_2 \cdot 2I_2$, $Zn(NH_3)_4I_2 \cdot 2I_2$, $Cd(NH_3)_4I_2 \cdot I_2$.

It must be pointed out that nickel iodide hexammine forms a polyiodide with a greater iodine content, even when no solvent is present.

Analogous investigations were conducted by Dawson and Gawler [4]. They studied the mutual solubility of iodine and potassium iodide in nitrobenzene in a considerable concentration interval, and according to the solubility data, found that potassium polyiodide KI_3—KI_9 is formed in nitrobenzene solutions at determined concentration conditions.

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* The ammines of nickel, zinc, and cadmium iodides are not soluble in alcohol and ether.

TABLE 1

Solubility of the Ammines in Nitrobenzene Solutions of Iodine

Moles of iodine / Moles of nitrobenzene	Moles of iodine / Moles of ammine in saturated sol.
Solubility of $Ni(NH_3)_6I_2$	
0.0082	3.20
0.0142	3.00
0.0189	2.92
Solubility of $Zn(NH_3)_4I_2$	
0.0115	2.10
0.0138	2.18
0.0237	2.11
Solubility of $Cd(NH_3)_4I_2$	
0.0062	1.90
0.0205	2.00
0.0250	1.96

TABLE 2

Solubility of the Ammines in Acetonitrile Solutions of Iodine

Moles of iodine / Moles of acetonitrile	Moles of Iodine / Moles of ammine in saturated solution
Solubility of $Ni(NH_3)_6I_2$	
0.0039	2.37
0.0059	2.36
0.0154	2.14
Solubility of $Zn(NH_3)_4I_2$	
0.0048	2.00
0.0076	2.06
0.0119	2.04
Solubility of $Cd(NH_3)_4I_2$	
0.0055	1.00
0.0093	1.13
0.0161	1.24

The results of the solubility determination unquestionably prove the fact of the formation of nickel, zinc, and cadmium ammine polyiodides in nitrobenzene and acetonitrile solutions, but they still cannot, however, answer the question of the actual structure, of the polyiodides formed in these solutions under the given conditions; it can be supposed that equilibria exist between the higher and lower polyiodides and free iodine; in this case the experimentally found molecular ratio between iodine and ammines (in solutions saturated with respect to the ammine) give only the "average" composition of the polyiodides, which changes very little with changes in the concentration of the iodine in solution.

Measurement of the electroconductivity. The solutions for the investigation were prepared directly in the vessel for the measurement of the electroconductivity. For this purpose, a weighed sample of iodine was added to a weighed sample of nitrobenzene; after the solution of the iodine and the measurement of the electroconductivity of the solution obtained, a series of weighed samples of the corresponding ammine were then introduced. The vessel was kept for some time at the given temperature and with periodic shaking; after the complete solution of the ammine, the electroconductivity of the solution was measured, and the measurement repeated after 20-30 minutes. The measurements were made at two temperatures: 25° and 35°.

The electroconductivity of solutions of iodine in nitrobenzene and acetonitrile at concentrations of 0.002-0.006 to 0.016-0.021 moles per mole of solvent were initially measured (Tables 3 and 4).

TABLE 3

Specific Electroconductivity of Iodine in Nitrobenzene

Moles I_2 / Moles $C_6H_5NO_2$	κ 25°	κ 35°
0.0061	$3.93 \cdot 10^{-6}$	$4.25 \cdot 10^{-6}$
0.0075	$5.45 \cdot 10^{-6}$	$5.70 \cdot 10^{-6}$
0.0088	$6.83 \cdot 10^{-6}$	$7.22 \cdot 10^{-6}$
0.0112	$7.94 \cdot 10^{-6}$	$8.36 \cdot 10^{-6}$
0.0139	$9.17 \cdot 10^{-6}$	$9.59 \cdot 10^{-6}$
0.0158	$1.00 \cdot 10^{-5}$	$1.06 \cdot 10^{-5}$

TABLE 4

Specific Electroconductivity of Iodine in Acetophenone

Moles I_2 / Moles CH_3CN	κ 25°	κ 35°
0.0018	$9.94 \cdot 10^{-5}$	$1.00 \cdot 10^{-4}$
0.0068	$1.09 \cdot 10^{-4}$	$1.11 \cdot 10^{-4}$
0.0131	$1.13 \cdot 10^{-4}$	$1.17 \cdot 10^{-4}$
0.0209	$1.31 \cdot 10^{-4}$	$1.37 \cdot 10^{-4}$

The values for the electroconductivity of solutions of iodine in nitrobenzene given in Table 3 are close to those which were found by Brunner and Galecki [5].[*] The electroconductivity of these solutions grows with the increase in the concentration of the iodine and reaches a value of the order of 10^{-5} ohm^{-1} cm^{-1}, i.e., very close to the electroconductivity of molten iodine with only this difference: the temperature coefficient of the electroconductivity of iodine solutions is positive.[**] This fact can serve as proof of the presence of ionic conductivity in nitrobenzene solutions of iodine caused by the electrolytic dissociation of the complex formed in these solutions.

Acetonitrile solutions of iodine conduct electricity considerably better (by 10-20 times), evidently, as a result of the formation in the system CH_3CN-I_2 of a more polar complex than in the system $C_6H_5NO_2-I_2$, analogous in its properties to the compound of pyridine with iodine for which the formula $[C_5H_5NI]^+I^-$ [6] must be accepted.

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[*] For this series of experiments, Brunner and Galecki used pure twice distilled nitrobenzene; which, after distillation was not kept from the moisture of the air. The authors call this preparation "wet".

[**] For molten iodine the temperature coefficient for the electroconductivity is negative.

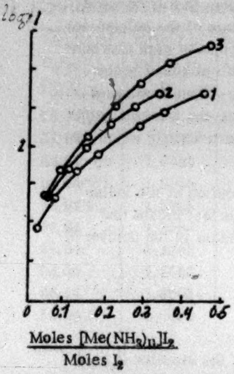

Fig. 1. Isotherms of the electroconductivity of nitrobenzene solutions of $\frac{\text{Moles } I_2}{\text{Moles } C_6H_5NO_2} = 0.0185$.
1 - [Cd(NH$_3$)$_4$]I$_2$; 2 - [Ni(NH$_3$)]$_6$I$_2$; 3 - [Zn(NH$_3$)$_4$]I$_2$.

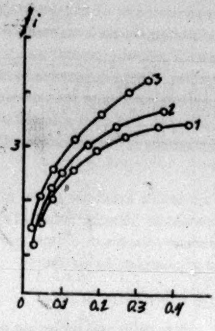

Fig. 2. Isotherms of the electroconductivity of acetonitrile solutions of $\frac{\text{Moles } I_2}{\text{Moles } CH_3CN} = 0.0114$.
1 - [Cd(NH$_3$)$_4$]I$_2$; 2 - [Ni(NH$_3$)$_6$]I$_2$; 3 - [Zn(NH$_3$)$_4$]I$_2$.

The results of the measurements of the electroconductivity of the ternary system metal iodide ammine—iodine—solvent (in order to save space) are only represented graphically on Figs. 1 and 2. Only for the system Ni(NH$_3$)$_6$I$_2$ - iodine-solvent are tabular results given in order to show, with this example, in more detail the character of the relation of the electroconductivity of the given systems to the concentration of the ammine and iodine (Tables 5 and 6).

As is apparent from Tables 5 and 6, and Figs. 1 and 2, the value of the specific electroconductivity of the ternary systems is characterized by the same concentration relationship: solutions more concentrated in relation to iodine at equal ratios of the metal iodides and iodine, show a greater electroconductivity value. At the same concentration of iodine, the electroconductivity of all these systems rises significantly with increase in the concentration of nickel, zinc, and cadmium iodide ammines, and acquires a value of the order of 10^{-3} ohm^{-1}cm^{-1} for nitrobenzene solutions and 10^{-2} ohm^{-1}cm^{-1} for acetonitrile solutions.

TABLE 5

Electroconductivity of the System Ni(NH$_3$)$_6$I$_2$—I$_2$—C$_6$H$_5$NO$_2$

$\frac{\text{Moles } I_2}{\text{Moles } C_6H_5NO_2}$	$\frac{\text{Moles Ni(NH}_3)_6I_2}{\text{Moles } I_2}$	$\kappa_{25°}$	$\kappa_{35°}$
0.0117	0.0289	$2.98 \cdot 10^{-4}$	$3.07 \cdot 10^{-4}$
0.0117	0.0949	$6.84 \cdot 10^{-4}$	$6.96 \cdot 10^{-4}$
0.0117	0.1612	$1.10 \cdot 10^{-3}$	$1.14 \cdot 10^{-3}$
0.0117	0.2231	$1.18 \cdot 10^{-3}$	$1.25 \cdot 10^{-3}$
0.0117	0.3598	$1.30 \cdot 10^{-3}$	$1.43 \cdot 10^{-3}$
0.0185	0.0317	$1.25 \cdot 10^{-4}$	$1.38 \cdot 10^{-4}$
0.0185	0.0699	$9.74 \cdot 10^{-4}$	$1.01 \cdot 10^{-3}$
0.0185	0.1216	$1.31 \cdot 10^{-3}$	$1.46 \cdot 10^{-3}$
0.0185	0.1746	$1.67 \cdot 10^{-3}$	$1.95 \cdot 10^{-3}$
0.0185	0.2521	$1.92 \cdot 10^{-3}$	$2.17 \cdot 10^{-3}$
0.0185	0.3330	$2.11 \cdot 10^{-3}$	$2.41 \cdot 10^{-3}$

TABLE 6

Electroconductivity of the System Ni(NH$_3$)$_6$I$_2$—I$_2$—CH$_3$CN

$\frac{\text{Moles } I_2}{\text{Moles } CH_3CN}$	$\frac{\text{Moles Ni(NH}_3)_6I_2}{\text{Moles } I_2}$	$\kappa_{25°}$	$\kappa_{35°}$
0.0064	0.0921	$6.30 \cdot 10^{-3}$	$6.33 \cdot 10^{-3}$
0.0064	0.1293	$7.48 \cdot 10^{-3}$	$7.56 \cdot 10^{-3}$
0.0064	0.1840	$8.79 \cdot 10^{-3}$	$8.97 \cdot 10^{-3}$
0.0064	0.2174	$9.19 \cdot 10^{-3}$	$9.48 \cdot 10^{-3}$
0.0064	0.2662	$9.77 \cdot 10^{-3}$	$1.12 \cdot 10^{-2}$
0.0114	0.0491	$5.92 \cdot 10^{-3}$	$6.00 \cdot 10^{-3}$
0.0114	0.0927	$8.59 \cdot 10^{-3}$	$8.73 \cdot 10^{-3}$
0.0114	0.1449	$1.13 \cdot 10^{-2}$	$1.16 \cdot 10^{-2}$
0.0114	0.2086	$1.38 \cdot 10^{-2}$	$1.43 \cdot 10^{-2}$
0.0114	0.2582	$1.66 \cdot 10^{-2}$	$1.71 \cdot 10^{-2}$
0.0114	0.3342	$1.77 \cdot 10^{-2}$	$1.81 \cdot 10^{-2}$

The investigated systems are also quite similar in the values of the electroconductivity at the same (or very close) concentration of iodine and ammine in the same solvents. Nevertheless, comparison of the isotherms shows that the systems with Zn(NH$_3$)$_4$I$_2$ possess a somewhat higher electroconductivity than systems with Ni(NH$_3$)$_6$I$_2$, and Cd(NH$_3$)$_4$I$_2$.

The electroconductivity of the systems with nitrobenzene are approximately 100 times, and the systems with acetonitrile, 10 times less than the electroconductivity of the corresponding binary systems, solutions of metal iodide ammines in molten iodine.

Cryoscopic measurements. Cryoscopic measurements of the system $Me(NH_3)_nI_2$-iodine in nitrobenzene as the solvent were conducted in order to further investigate the composition and the structure of the polyiodides. These measurements were made in an apparatus with ground glass stoppers. The freezing point of pure nitrobenzene was first measured with a Beckmann thermometer, then a determined amount of iodine was added to the nitrobenzene and freezing point depression of nitrobenzene due to iodine* was determined. Then, a series of weighed samples of ammines were added to the solution, and after solution of these samples, the freezing point of the solution determined with increasing concentrations of the ammines. Only those experiments in which the supercooling did not exceed 0.1° were noted.

The addition of nickel, zinc, and cadmium iodide ammines to the nitrobenzene solution of the iodine first causes a decrease in the depression (i.e., increase in freezing point) (Tables 7-9). This fact means that the solution of the given ammines in the nitrobenzene solution of iodine results in the decrease in the number of particles in the solution as a result of the process of complex formation:

$$[Me(NH_3)_n]I_2 + mI_2 = [Me(NH_3)_n]I_2 \cdot (I_2)_m,$$

which causes the binding of several molecules of iodine with one molecule of the iodide.

The change of the freezing point of the solution in relation to the concentration of the ammine is most expediently represented graphically by placing on the abscissas

$$\frac{\text{Moles } [Me(NH_3)_n]I_2 \cdot 100}{\text{Moles } [Me(NH_3)_n]I_2 + \text{Moles } I_2}$$

on the ordinates, the change in the freezing point (Δt_2 in Tables 7-9) caused by the solution of the ammine in the nitrobenzene solution of the iodine. Such a graphic representation of the cryoscopy data of the ternary system of the type A-B-solvent [8], makes the use of cryoscopy as a method for the physico-chemical analysis of these systems possible.

TABLE 7

Cryoscopy of the System $C_6H_5NO_2-I_2-Ni(NH_3)_6I_2$

Weight of $C_6H_5NO_2$ (in g)	Weight of iodine (in g)	Weight of $Ni(NH_3)_6I_2$ (in g)	$\frac{\text{Moles } Ni(NH_3)_6I_2 \cdot 100}{\text{Moles } Ni(NH_3)_6I_2 + \text{Moles } I_2}$	Freezing point	Δt_1°	Δt_2°
53.91	–	–	–	4.610	–	–
53.91	1.0891	–	–	4.062	0.548	–
53.91	1.0891	0.0482	2.64	4.106	0.504	−0.044
53.91	1.0891	0.1128	5.83	4.157	0.453	−0.095
53.91	1.0891	0.2000	10.11	4.200	0.410	−0.138
53.91	1.0891	0.3104	14.85	4.189	0.421	−0.127
53.91	1.0891	0.3814	17.65	4.165	0.445	−0.103
53.91	1.0891	0.5058	22.13	4.136	0.474	−0.074
53.91	1.0891	0.6047	25.20	4.104	0.506	−0.042

TABLE 8

Cryoscopy of the System $C_6H_5NO_2-I_2-Zn(NH_3)_4I_2$

Weight of $C_6H_5NO_2$ (in g)	Weight of iodine (in g)	Weight of $Zn(NH_3)_4I_2$ (in g)	$\frac{\text{Moles } Zn(NH_3)_4I_2 \cdot 100}{\text{Moles } Zn(NH_3)_4I_2 + \text{Moles } I_2}$	Freezing point	Δt_1°	Δt_2°
45.40	–	–	–	4.425	–	–
45.40	0.6627	–	–	4.034	0.391	–
45.40	0.6627	0.0290	2.79	4.066	0.359	−0.032
45.40	0.6627	0.0451	4.16	4.075	0.350	−0.041
45.40	0.6627	0.0958	8.65	4.111	0.314	−0.077
45.40	0.6627	0.1461	12.62	4.138	0.287	−0.104
45.40	0.6627	0.2112	17.28	4.151	0.274	−0.117
45.40	0.6627	0.2533	20.03	4.156	0.269	−0.122
45.40	0.6627	0.3143	23.71	4.148	0.277	−0.114
45.40	0.6627	0.3851	28.90	4.122	0.303	−0.088

* The molecular weight of iodine calculated in the benzene solution gave an average value of 254.3 which agrees with the literature data [7].

TABLE 9

Cryoscopy of the System $C_6H_5NO_2-I_2-Cd(NH_3)_4I_2$

Weight of $C_6H_5NO_2$ (in g)	Weight of iodine (in g)	Weight of $Cd(NH_3)_4I_2$ (in g)	$\frac{\text{Moles } Cd(NH_3)_4I_2 \cdot 100}{\text{Moles } Cd(NH_3)_4 + \text{Mole } I_2}$	Freezing point	Δt_1°	Δt_2°
56.94	–	–	–	4.425	–	–
56.94	1.3055	–	–	3.898	0.527	–
56.94	1.3055	0.0275	1.22	3.952	0.473	−0.054
56.94	1.3055	0.0763	3.30	3.971	0.454	−0.073
56.94	1.3055	0.1344	5.68	4.017	0.408	−0.119
56.94	1.3055	0.2005	8.24	4.064	0.361	−0.166
56.94	1.3055	0.3059	12.04	4.102	0.323	−0.204
56.94	1.3055	0.4119	15.57	4.092	0.333	−0.194
56.94	1.3055	0.5017	18.34	4.063	0.362	−0.165
56.94	1.3055	0.6288	21.96	4.018	0.407	−0.120

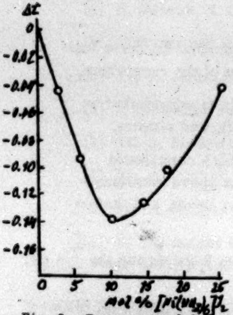

Fig. 3. Cryoscopy of the system $C_6H_5NO_2-I_2-[Ni(NH_3)_6]I_2$

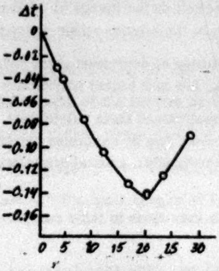

Fig. 4. Cryoscopy of the system $C_6H_5NO_2-I_2-[Zn(NH_3)_4]I_2$

Decrease in the depression of the solution, occurring during the addition of $[Me(NH_3)_n]I_2$ to the nitrobenzene solution of iodine, proceeds only to a certain minimum value corresponding to the achievement of a determined molar ratio of ammine and iodine. Upon the further addition of the ammine, the freezing point begins to decrease again (the depression increases), as it is apparent from Tables 7-9 and Figs. 3-5 in which the cryoscopy results of the system $[Me(NH_3)_n]I_2$–iodine–nitrobenzene are presented graphically. Therefore, with the increase in the concentration of the ammine, the number of particles in the solution decreases at first and then, on achieving a certain minimum value, begins to increase.

This type of change in the depression of the system of the type A–B–solvent occurring on the addition of component B to a solution of component A, has already been mentioned in the literature, as for example during the investigation of the systems: iodine chloride–acetamide–nitrobenzene [9], iodine chloride–potassium chloride–nitrobenzene [10] and certain others [8].

In the systems here studied such a decrease in the depression with the increase in the concentration of ammine (and the inflection on the depression change curve) was found up to the achievement of such a ratio of $\frac{\text{Moles } [Me(NH_3)_n]I_2 \cdot 100}{\text{Moles } [Me(NH_3)_n]I_2 + \text{Mole } I_2}$, which is found to be ~ 11% for the systems with $Ni(NH_3)_6I_2$, ~ 20 mole % for the systems with $Zn(NH_3)_4I_2$, and ~ 14 mole % for the systems with $Cd(NH_3)_4I_2$.

As the results of the above reported investigation on the solubility of $[Me(NH_3)_n]I_2$ in nitrobenzene solutions of iodine and on the electroconductivity of the systems obtained show, in the systems $[Me(NH_3)_n]I_2$–iodine–solvent, a process of complex formation leading to a decrease in the number of particles in the solution as well as a process of dissociation of the complex resulting in an increase in the total number of particles in the solution, occurs.

With relatively small concentrations of the ammine in the solution there is a great excess of iodine which creates conditions favorable for the formation of the polyiodide $[Me(NH_3)_n]I_2 \cdot (I_2)_m$, more rich in iodine and more stable under the given conditions of the experiment. With the addition of more ammine, more iodine is bound in the form of the polyiodide, and when a quantity of ammine sufficient to combine with the iodine in the solution as the more rich in iodine (under conditions of the experiment) polyiodide has been added, the total number of particles in the solution will be the smallest, which is shown by the lowest value for the depression on the curve of the change of the depression with the concentration of the ammine

The higher polyiodides formed in the solution, evidently, are subjected to a gradual dissociation; therefore there must exist an equilibrium between the higher and lower polyiodides and the free iodine molecules in the solution according to the scheme:

$$[Me(NH_3)_n]I_2 \cdot (I_2)_m \rightleftharpoons [Me(NH_3)_n]I_2 \cdot (I_2)_{m-1} + I_2 \rightleftharpoons [Me(NH_3)_n]I_2 \cdot (I_2)_{m-2} + 2I_2, \text{etc.}$$

For this reason, upon the further addition of the ammine, the above equilibrium is shifted to the right, i.e., polyiodides less rich in iodine are formed in the solution, which leads to an increase in the total number of particles in the solution, for example:

$$Ni(NH_3)_6I_2 \cdot (I_2)m + Ni(NH_3)_6I_2 \quad = \quad Ni(NH_3)_6I_2 \cdot (I_2)m-n + Ni(NH_3)_6I_2 \cdot (I_2)n, \text{etc.}$$

When the increase in the number of particles, caused by such a processess, as well as by the electrolytic dissociation of the polyiodides, begins to predominate over the decrease of the number of molecules of iodine in the solution as a result of complex formation, the decrease in the depression is stopped, and the freezing point of the solution starts to drop, although the freezing point may still be higher than that of the starting solution of iodine in nitrobenzene, as was observed in these experiments. *

Therefore, it can be said that the inflection on the change of depression with concentration curve indicates the composition of the higher polyiodide in the solution stable under the conditions of the experiment.

The position of the minimum on the change of depression curve makes it possible to suggest that $Ni(NH_3)_6I_2 \cdot 8I_2$, $Zn(NH_3)_4I_2 \cdot 4I_2$, $Cd(NH_3)_4I_2 \cdot 6I_2$, are such higher polyiodides in the investigated systems.

The slight error in the theoretical composition of these polyiodides, from that which corresponds to the inflection on the change of depression curve, can be explained by the effect of the above mentioned processes: formation of associated polyiodide molecules, gradual dissociation of the complexes, and their electrolytic dissociation.

The composition of these polyiodides is very close to those complexes which were found during the investigation of the binary systems:

$[Me(NH_3)_n]I_2$—iodine, namely, $[Ni(NH_3)_6](I_9)_2$, $[Zn(NH_3)_4](I_5)_2$ and $[Cd(NH_3)_4](I_5)_2$—$[Cd(NH_3)_4](I_7)_2$.

Comparison of the experimental results on the solubility of nickel, zinc, and cadmium iodide ammines in nitrobenzene and acetonitrile solutions of iodine, as well as the electroconductivity and cryoscopy of the systems formed, shows that the ammine polyiodides of these metals are formed in organic solvents as in the corresponding binary systems of $[Me(NH_3)_n]I_2$—iodine, whereby the high electrolytic properties of these polyiodides are retained in the organic solvents investigated, with the only difference being that the value of the electroconductivity decreases with the dilution.

Therefore, the results of the present investigation, as well as those of the above mentioned binary systems are in agreement with the positions expressed in the literature, which conclude that solvents more or less indifferent to components of a binary system do not change the character of a reactant with the components of the binary system but only weaken the magnitude of the properties (have an effect analogous to the temperature) [11].

The results of the cryoscopic investigation of the system $[Me(NH_3)_n]I_2$—iodine—nitrobenzene showed that the cryoscopic method of physico-chemical analysis [8] can be extended to systems of the type A-B-solvent, one of the components of which (A or B), not soluble in the given solvent, dissolves in it only in the presence of the second component because of the appearance of complex formation.

SUMMARY

1. Nickel, zinc, and cadmium iodide ammines which are almost insoluble in nitrobenzene and acetonitrile, dissolve in nitrobenzene and acetonitrile solutions of iodine. The molar ratio of the iodine in the solution

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* This fact may be the result of the association of the polyiodide molecules in the nitrobenzene solution.

and these amounts of nickel, zinc, and cadmium iodide ammines which went into solution (up to saturation) remains almost constant for each of the given ammines, even if the concentration of iodine in the initial solution is changed by 3-4 times, and corresponds to the formation of determined polyiodides.

2. The electroconductivity of the systems $Ni(NH_3)_6I_2$, $Zn(NH_3)_4I_2$, and $Cd(NH_3)_4I_2$ – iodine – nitrobenzene (or acetonitrile) was measured. The electroconductivity of these systems, caused by the electrolytic dissociation of the polyiodides formed in them, is about 10^{-2} for solutions in acetonitrile and 10^{-3} ohm^{-1} cm^{-1} for nitrobenzene solutions.

3. The cryoscopic investigation of the systems, consisting of the ammines of nickel, zinc, and cadmium iodines and iodine in nitrobenzene solutions gave a basis for supposing that the higher polyiodides formed in these systems are, respectively:

$Ni(NH_3)_6I_2 \cdot 8I_2$, $Cd(NH_3)_4I_2 \cdot 6I_2$ and $Zn(NH_3)_4I_2 \cdot 4I_2$

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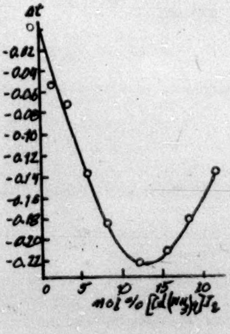

Fig. 5. Cryoscopy of the system $C_6H_5NO_2 - I_2 - [Cd(NH_3)_4]I_2$.

PHYSICO-CHEMICAL ANALYSIS OF BINARY SYSTEMS FORMED BY UREA WITH AROMATIC ACIDS

N. Z. Rudenko and D. E. Dionisyev

Continuing the work on the study of the reaction of urea with organic components containing hydrogen atoms combined directly with an oxygen, the binary systems formed by urea and the aromatic acids, benzoic, salicylic, and anthranilic, were investigated. The viscosity, density, and electroconductivity of the systems were investigated at three temperatures.

The choice of the second components was determined by a desire to find out what will be the effect of the presence of an aromatic ring, and the introduction of a hydroxy and amino group into the aromatic ring on the character of the chemical reaction with urea.

The method of investigation was the same as had previously been used [1]. The concentration is in molecular percent, the viscosity in centipoises.

The system urea-benzoic acid was studied by melting points by a series of investigators [2,3]. They came to the conclusion that a chemical reaction between the components did not occur in the system. The viscosity, density, and electroconductivity were investigated by the authors of the present communication at 120, 135, and 150°.

Chemically pure benzoic acid which had a m.p. 121.1° after redistillation, was used for the investigation. The urea, after many recrystallizations from water, had a m.p. 132.7°. Fig. 1 shows the relation of the viscosity to the temperature. The viscosity curves rise rapidly as a result of the viscosity of benzoic acid, pass through a maximum, and decrease to the viscosity of urea. The viscosity maximum for the 120° isotherm corresponds to 60 mole % of urea. With increase in temperature, it is still more shifted toward the more viscous component, urea, and for the 150° isotherm, corresponds to 70 mole % of urea. The temperature coefficient of viscosity is also greatest for the region of 50 mole % of urea.

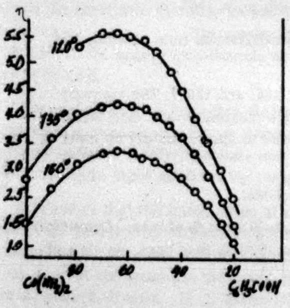

Fig. 1. Viscosity of the system urea — benzoic acid.

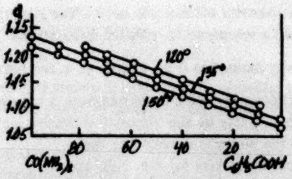

Fig. 2. Density of the system urea — benzoic acid.

Fig. 2 gives the density isotherms which are straight lines.

The electroconductivity isotherms have a total of two maxima and a minimum in the region of 50 mole %. Correcting the electroconductivity by the viscosity does not change the shape of the curve. All three isotherms retain a minimum at approximately the region of 50 mole %. Fig. 3 shows the relation of the isotherm $\eta\kappa$ to the composition, giving only that part of the curve with the minimum. Not shown on Fig. 3 is the maximum for the isotherm corresponding to approx. 90 mole % of urea, and being for the 135° isotherm $\eta\kappa = 28.52 \cdot 10^4$, and for the 150°, $\eta\kappa = 24.79 \cdot 10^4$, (for urea, $\eta\kappa$ is about $7 \cdot 10^4$).

The system urea—salicylic acid was investigated by Kremann, Weber, and Zechner [2] by means of melting points. They showed the presence of one compound of urea and salicylic acid. The system was also investigated by means of melting points [4] by the authors, and two compounds were found: $CO(NH_2)_2 \cdot C_6H_4(OH)COOH$ with m. p. 112° and $2CO(NH_2)_2 \cdot C_6H_4(OH)COOH$ with m. p. 106°.

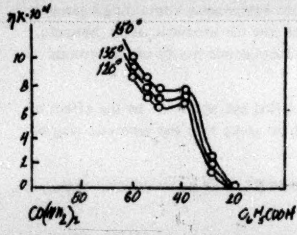

Fig. 3. Values of ηκ for the system urea—benzoic acid.

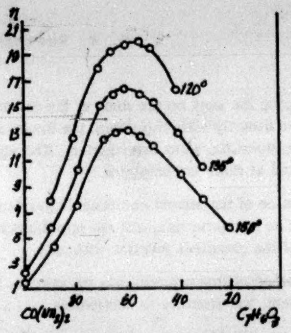

Fig. 4. Viscosity of the system urea—salicylic acid.

Chemically pure salicylic acid which had a m. p. 156° after two recrystallizations from alcohol, was used.

The viscosity, density, and electroconductivity were measured at 120, 135, and 150°. The viscosity isotherms, given in Fig. 4, rise rapidly from the viscosity of urea, pass through a maximum, and then fall just as rapidly to the viscosity of salicylic acid. The viscosity maximum corresponds to approximately 50 mole %, and with increase in temperature, readily shifts toward urea.

The density isotherms (Fig. 5) are, as in the previous systems, straight lines.

The electroconductivity isotherms have a maximum in the region of 85-90 mole % of urea. Correction of the electroconductivity by the viscosity shifts the maximum of the curve to 75 mole % of urea. In view of the similarity of the numerical values of the corrected electroconductivity for 120, 135, and 150°, Fig. 6 gives only the 135° isotherm.

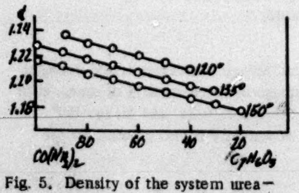

Fig. 5. Density of the system urea—salicylic acid.

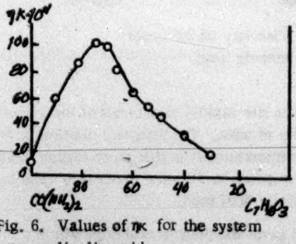

Fig. 6. Values of ηκ for the system urea—salicylic acid.

The system urea—anthranilic acid was studied previously [4] by means of melting points. A melting point diagram with a simple eutectic was obtained.

In this system, only the electroconductivity could be investigated; the viscosity could not be investigated because of the slow continuous separation of gas bubbles which filled the capillary and made the measurement erroneous.

Chemically pure anthranilic acid which had an m.p. 145° after three recrystallizations from water, was used.

The specific electroconductivity was measured at 115°, 130°, and 145°.

Fig. 7 shows the relation of the electroconductivity to the concentration. The electroconductivity isotherm rises smoothly to that of urea, and the 140° isotherm passes through a maximum at 90 mole %. Apparently, all of the other isotherms must pass through a maximum in this region at this concentration. Because of the crystallization of the mixture, the isotherms could be measured up to 80 mole % of urea at 115°, and 90 mole % at 130°.

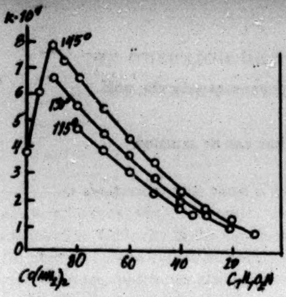

Fig. 7. Electroconductivity of the system urea-anthranilic acid.

DISCUSSION OF RESULTS

In the system urea-benzoic acid, the viscosity isotherms which have not only a positive deviation, but also a maximum, as well as the electroconductivity isotherm which has a minimum, undoubtedly indicate the presence of a chemical reaction in the system. The position of the maximum on the viscosity curve and the minimum on the electroconductivity curves, leads to the belief that the reaction in the system results in the formation of the compound $CO(NH_2)_2 \cdot C_6H_5COOH$, which was not observed by the melting point method. It is interesting that in the system benzoic acid-salicylic acid, a compound of the composition 1:1 was also found in the liquid phase [5], whereas the fusion diagram has only a simple eutectic.

Because of the hydroxy group in the ring, the tendency to react is increased, which is apparent from the data of the system urea-salicylic acid. The viscosity isotherms of this sytem have a distinct maximum in the region of 50 mole %. A rough idea of the percent completion of the chemical reaction can be obtained from the ratio of the maximum viscosity to that of the most viscous component which is common to both systems, in the given case. The greater the quotient, the more intense the reaction. Such a ratio for the viscosity at 135° in the system urea-benzoic acid is equal to 1.58, and for the same temperature, 6.22 for the system urea-salicylic acid.

The isotherm of the corrected electroconductivity, having a maximum in the region of 75 mole % of urea, can be said to express the presence of the compound $2CO(NH_2)_2 \cdot C_6H_4(OH)COOH$ in the system, while the viscosity isotherm readily expresses the compounds $CO(NH_2)_2 \cdot C_6H_4(OH)COOH$. Therefore, a study of the system in the liquid phase confirms the presence of two compounds of urea and silicylic acid.

It is known that the introduction of an amino group into the ring decreases the strength of acids, which must affect the reaction of urea and anthranilic acid. Actually, it was shown by means of the fusion method that a chemical reaction was absent in the system [4].

A study of the system in the liquid phase by electroconductivity showed that these curves have a maximum at 90 mole % of urea. M. I. Usanovich considers that the appearance of such electroconductivity curves indicates an acid-base reaction between the components of the system [6]. By the position of the maximum, it is, of course, difficult to judge the composition of the chemical compound.

It must be mentioned that, upon prolonged heating of a mixture of urea with benzoic, salicylic, and anthranilic acid at a composition close to 50 mole % at temperatures over 150°, carbon dioxide and ammonia are evolved and substances difficultly soluble in water, dilute acids and bases, alcohol, ether, and other organic solvents, are formed.

SUMMARY

1. The viscosity, density, and electroconductivity of the systems urea-benzoic acid, urea-salicylic acid, were studied at 120, 135, and 150°, and the electroconductivity of the system urea-anthranilic acid at 115, 130, and 145°.

2. The presence of a chemical reaction in the liquid phase was shown for the system urea-benzoic acid,

evidently, with the formation of the compound $CO(NH_2)_2 \cdot C_6H_5COOH$.

3. The presence of two compounds was shown in the liquid phase of the system urea-salicylic acid, $CO(NH_2)_2 \cdot C_6H_4(OH)COOH$ and $2CO(NH_2)_2 \cdot C_6H_4(OH)COOH$.

4. In the system, urea-anthranilic acid, the presence of an acid base reaction can be assumed.

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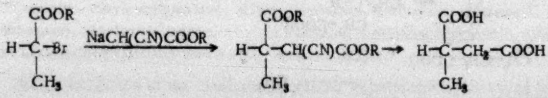
THE QUESTION OF THE DETERMINATION OF CONFIGURATION OF MOLECULES WITH TERTIARY ASYMMETRIC CARBON ATOMS

V. P. Golmov

At the present time there is no chemical method for the determination of configuration of optically active substances whose molecules contain an asymmetric carbon atom combined with three other carbon atoms. The difficulty in the determination of configuration in the given case is the fact that substances of the above structure cannot be obtained from glyceraldehyde without a stage of substitution in the asymmetric center, which can always be accompanied by a Walden inversion making it impossible to make any conclusion on their configuration. For this reason, attempts to determine the configuration of such substances using methods with substitution at the asymmetric atom are unsuccessful, which was shown by the authors of this investigation. The above applies, for example, to the determination of configuration of stereoisomers of methylsuccinic acid, used by E. Fischer [1], starting from an α-bromopropionic acid of known configuration:



$$H-\overset{COOR}{\underset{CH_3}{C}}-Br \xrightarrow{NaCH(CN)COOR} H-\overset{COOR}{\underset{CH_3}{C}}-CH(CN)COOR \rightarrow H-\overset{COOH}{\underset{CH_3}{C}}-CH_2-COOH$$

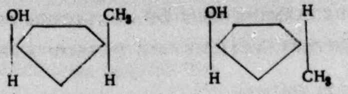
as well as the attempt of J. Braun [2] to determine the configuration of β-methyladipic acid in order to establish the configuration of the natural terpene molecules.

Recently, Fregda used a method, starting with a substance of opposite structural configuration, for the determination of configuration of compounds having tertiary asymmetric carbon atoms to give the so-called "active racemates", the formation of which can be judged by using fusion curves of a system one of whose components is the compound of known configuration, and the other, that being studied. Using this method, Fregda established the true configuration of stereoisomeric methyl succinic [3], isopropylsuccinic [4], β-isopropyladipic [5] acids, and a series of other compounds derived from them, starting from active malic acid of known configuration. The results of this method, like other physical methods, can only determine the true configuration of active compounds; in addition, he used only solid substances for determination of configuration.

Evidently, in order to make possible the determination of configuration of substances with tertiary asymmetric carbon atoms chemically, it is necessary to discard the usual methods for comparison of configuration based on the transition from one of the stereoisomeric forms of glyceraldehyde to the given substance, or the reverse [6]; in its place a new method must be sought for the comparison of configuration free from the necessity of having to effect substitution on the asymmetric center. The following can be used in this manner. Glyceraldehyde on the one hand, and the substance whose configuration is being determined, on the other, have to be related to each other by means of exchange reactions with those cyclic compounds that have 2 centers of asymmetry in the ring. The first of these centers of asymmetry must originate from one of the forms of glyceraldehyde, and the configuration of the substituents around it, therefore, must be known. The second asymmetric carbon atom must be genetically combined to the center of asymmetry of the molecule of the substance whose configuration is being determined. Then the configuration of the substituent around this asymmetric atom is determined on the basis of whether the substituents in both centers are found in cis or trans position to each other.

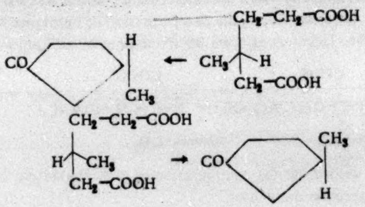
Let the above be explained by the following example. Let us suppose that the determination of the configuration of the enantiomorphic β-dimethyladipic acids is desired, starting from the d- and l- forms of glyceraldehyde of known configuration. The direct transition from glyceraldehyde to β-methyladipic acid is, evidently, impossible without disturbing the asymmetric center.

However, if one of the active forms of glyceraldehyde could be related by a series of subsequent transformation to the configuration, for example, of 3-methylcyclopentanol, two diastereomers will be obtained as a result:



which would be cis and trans isomers at the same time.

Since the configuration of substituents at the center of asymmetry combined with the hydroxyl group would be known, the position of the substituent around the other asymmetric carbon atom determines the category of the diastereomer as cis or trans. Oxidizing both diastereomeric 3-methylcyclopentanols into ketones, two enantiomorphic 3-methylcyclopentanones with molecules of known configuration will be obtained. Since, on the other hand, these ketones can be obtained from the corresponding active β-methyladipic acids [7], the configuration of the latter will be established:



SUMMARY

The problem of determining the configuration of substances which cannot be obtained from glyceraldehyde without disturbing the center of asymmetry is almost completely solved and only the removal of a series of difficulties, experimental in character, remains. A possible means for the determination of configuration of β-methyladipic acid is given.

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CATALYTIC ISOMERIZATION OF UNSATURATED HYDROCARBONS

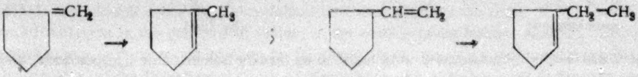
XIX. ISOMERIZATION OF UNSATURATED FIVE- AND SIX-MEMBERED CYCLIC HYDROCARBONS WITH A DOUBLE BOND IN THE SIDE CHAIN

R. Ya. Levina, N. N. Mezentsova, and P. A. Akishin

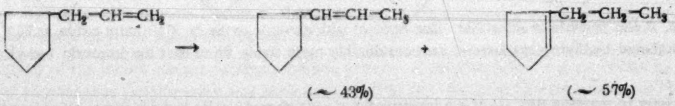
The rearrangement of a double bond under the influence of a contact catalyst has been reported in the literature for only a few examples of cyclic hydrocarbons with a double bond in the ring or in the side chain, in contrast to the isomerization of unsaturated hydrocarbons with an open side chain [1]. Thus, O. G. Filippov [2] brought about the rearrangement of methylenecyclobutane into 1-methylcyclobutene-1 by passing it over aluminum oxide (300°). The rearrangement of the ring double bond in 1-methyl-4-isopropylcyclohexene-1 (menthene-1) by contact with magnesium sulfate on copper phosphate (300-450°) has been reported; under these conditions menthene-1 rearranged into menthene-3 (1-methyl-4-isopropylcyclohexene-3) [3].

A systematic investigation was conducted during the present study of the catalytic isomerization of certain five membered and six membered cyclic hydrocarbons with a double bond in the ring or in the side chain: methylenecyclopentane, vinylcyclopentane, allylcyclopentane, 1-ethylcyclopentene-1, 1-ethylcyclopentene-2, methylenecyclohexane, vinylcyclohexane, allylcyclohexane, 1-ethylcyclohexene-1, and 1-ethylcyclohexene-2. Chromic oxide on aluminum oxide was used as the contact catalyst.*

The investigation of the catalyzates obtained was effected by means of Raman spectra. It was established that, with one pass over chromic oxide on aluminum oxide at 250°, methylene and vinylcyclopentane rearranged completely; the catalyzate obtained did not contain the starting α-ethylenic hydrocarbons and consisted of the isomeric alkylcyclopentenes-1, 1-methyl- and 1-ethylcyclopentene-1, respectively:

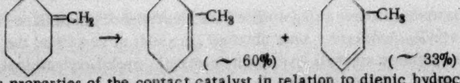


Allylcyclopentene, in which the double bond is farther from the ring, rearranged completely after only two passes over the contact catalyst to form two isomeric hydrocarbons, transpropenylcyclopentane and 1-propylcyclopentene-1:



Therefore, the sequence of the rearrangement of the double bond into the ring is shown by the example of allylcyclopentane.

Cyclohexane hydrocarbons with unsaturated side chains, methylene, vinyl, and allylcyclohexane, were rearranged by one pass over chromic oxide on aluminum oxide at 250° mainly into the 1-alkylcyclohexene-1. However, in this case, in contrast to the isomerization of the alkenecyclopentanes, a further isomerization of the 1-alkylcyclohexenes-1 into 1-alkylcyclcohexenes-2 (possibly with a trace of 1-alkylcyclohexene-3) occurred. Such a rearrangement of the double bond in the ring occurred to a greater extent with methylene cyclohexane than with vinyl and allylcyclohexane.



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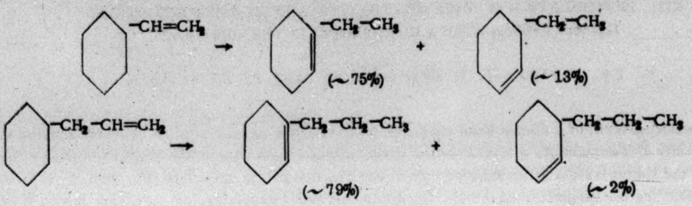
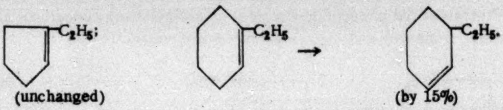
* The high isomerization properties of the contact catalyst in relation to dienic hydrocarbons, as well as aromatic hydrocarbons with unsaturated side chains was shown in previous investigations [4, 5, 6].

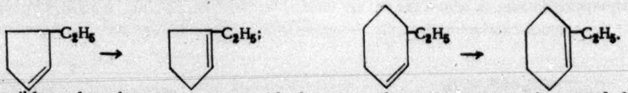


It was of interest to study further the behavior, under the above conditions, of the products of these reactions, 1-alkylcycloalkenes-1, as well as hydrocarbons isomeric with them, the 1-alkylcycloalkenes-2 in which the double bond is farther away from the substituent. For this purpose, 1-ethylcyclopentene-1 and 1-ethylcyclohexene-1, as well as 1-ethylcyclopentene-2 and 1-ethylcyclohexene-2 were subjected to contact catalysis over chromic oxide on aluminum oxide at 250°.

1-Ethylcyclopentene-1 was found to be exceptionally stable under conditions of contact isomerization: upon passing it over the contact catalyst at 250°, it was almost unchanged, while its six-membered analog, 1-ethylcyclohexene-1, under these conditions, suffered a partial (~15%) isomerization with the rearrangement of the double bond in the ring into a position farther away from the alkylated carbon atom.

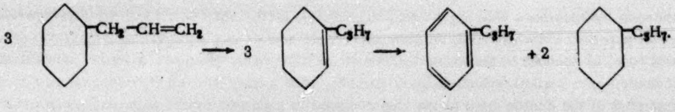


1-Ethylcyclopentene-2 and 1-ethylcyclohexene-2 were found to be readily isomerizable hydrocarbons, and under the contact conditions, rearranged (by~ 40-50%) into 1-alkylcycloalkenes-2 (with the movement of the double bond in the ring toward the alkylated carbon atom):



Therefore, it was possible to show that, upon contact with chromic oxide on aluminum oxide at 250°, five- as well as six-membered 1-alkylcycloalkenes-1 are considerably more stable forms that the isomeric 1-akylcycloalkenes-2.

It is necessary to mention that all of the investigated six-membered cyclic hydrocarbons, alkenecyclohexane and alkylcyclohexenes under the conditions of contact isomerization (chromic oxide on aluminum oxide at 250°) partially underwent an irreversible N.D. Zelinsky rearrangement, for example:



EXPERIMENTAL

The starting cyclic hydrocarbons without a ring double bond, methylenecyclopentane, methylenecyclohexane, vinylcyclopentane, and vinylcyclohexane* were obtained (in yields of 70-85% of the theoretical) by the pyrolysis of the acetates of the primary alcohols, cyclopentylcarbinol, cyclohexylcarbinol, and cyclohexylethanol, synthesized by the reaction of paraformaldehyde or ethylene oxide with cyclopentyl or cyclohexyl magnesium chloride. The constants of the alcohols and acetates obtained are given in Table 1.

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* The syntheses of the hydrocarbons were reported in detail in one of the previous communications [7]. Recently, a synthesis of these hydrocarbons was published [8] without quoting this paper.

TABLE 1

Name	Boiling point	n_D^{20}	d_4^{20}	MRD		Yield (in % of theoretical)
				Found	Calculated	
Cyclopentylcarbinol	58-59° (14-15 mm)	1.4579	0.9332	29.28	29.23	30
Acetate	85-86 (40 mm)	1.4378	0.9574	38.97	38.59	70
Cyclohexylcarbinol	88-89 (11-12 mm)	1.4656	0.9285	34.03	33.85	35
Acetate	75-76 (14-15 mm)	1.4460	0.9605	43.36	43.21	73
Cyclopentylethanol	74 (12-13 mm)	1.4578	0.9231	33.74	33.85	40
Acetate	75 (14-15 mm)	1.4408	0.9504	43.38	43.21	75
Cyclohexylethanol	99-100 (15 mm)	1.4649	0.9189	38.58	38.47	33
Acetate	97-98 (15 mm)	1.4478	0.9500	47.97	47.83	80

Allylcyclopentane and allylcyclohexane were obtained by the action of allyl chloride on cyclopentyl magnesium chloride and cyclohexyl magnesium chloride.

1-Ethylcyclopentene-2 and 1-ethylcyclohexene-2 were synthesized (in yields of 50 and 54% of the theoretical) by the reaction of ethyl magnesium bromide with 1-chlorocyclopentene-2 and 1-bromocyclohexene-2, which were obtained by the action of hydrogen halides on cyclopentadiene and cyclohexadiene-1,3, respectively. The hydrohalides of cyclopentadiene and cyclohexadiene-1,3 (as soon as they were obtained) were reacted with ethyl magnesium bromide, used in some excess (~ 30%).

1-Ethylcyclopentene-1 and 1-ethylcyclohexene-1 were obtained (in yields of 55 and 48% of the theoretical) by the dehydration (distillation in the presence of iodine) of the corresponding tertiary alcohols. Other cyclopentyl and cyclohexenyl hydrocarbons with the same position for the double bond (1-methyl- and 1-propylcycloalkenes-1), possible isomerization products of the investigated cyclic hydrocarbons with a double bond in the side chain, were obtained in the same way. The constants of all of the synthesized hydrocarbons (after distillation over sodium through a column of 30 theoretical plates) are given in Tables 2 and 3.

The hydrocarbons were passed over chromic oxide on aluminum oxide (tube diameter 16 mm), length of catalyst layer, 45 cm) at 250° in a slight stream of nitrogen at a rate of 0.06 g/minute. The catalyzates (yield 80-85%) distilled completely with the limits of temperature given in Tables 2 and 3. (The distillation was conducted over sodium from a flask with a small dephlegmator); higher boiling fractions were absent.

The activity of the mixed contact catalyst, chromic oxide on aluminum oxide, was controlled by the degree of isomerization of allylbenzene (allylbenzene was isomerized by 95%) [4]. Before each experiment, the contact catalyst was activated by heating with a stream of air for 4-5 hours at 450°.

The synthesized hydrocarbons and the catalyzates obtained from them (I-X) were investigated by Raman spectra; the Raman spectra were taken on a three prism spectrograph with glass optics having an average dispersion of 13 A/mm in the region of 4385-4916 A with a slit width of 0.1 mm (~6 cm^{-1} on the spectrum). The spectrum was excited by the 4358 A line (spectrofilter with KNO_3). The method of photography, measurement of the frequencies, calculation of the intensity of the lines, and the composition of the components in the mixture were previously described in detail [9-10].

The application of the Raman spectrum for the study of the rearrangement processes of double bonds in unsaturated cyclic hydrocarbons is based on the characteristic frequencies in the region 1640-1680 cm^{-1} for the isomeric cyclic hydrocarbons with different positions of the double bond. The constants of the catalyzates and the characteristic frequencies of their double bond in the Raman spectrum are given in Tables 2 and 3.

Comparison of the spectra of individual hydrocarbons* with those of the catalyzate and the use of the characteristic frequencies, made it possible to establish a qualitative composition of the catalyzate obtained after the passage of each hydrocarbon over the contact catalyst.

The determination of the quantitative composition of the separate components in the catalyzate was effected

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* The set of analytically important frequencies (in the region $\omega \sim$ 200-1680 cm^{-1} of the Raman spectrum of all of the investigated hydrocarbons are given in the previous communication [11].

TABLE 2

Hydrocarbons and catalyzates	Boiling point	n_D^{20}	d_4^{20}	Characteristic frequency of the C=C bond in the Raman spectrum cm^{-1}	Composition of the catalyzate	Frequency line used for the determination
Methylene cyclohexane	99.8-100° (766 mm)	1.4498	0.8055	1651	—	—
Catalyzate VI (After passing methylenecyclohexane over the contact catalyst)	104 -106 (747 mm)	1.4490	0.8088	1651 1676	1-Methylcyclohexene-∼60% 1-Methylcyclohexene-2 ∼33% (with a possible contamination with 1-methylcyclohexene-3)** Toluene∼1.5-2.0% Methylcyclohexane∼5%	1676 1651* 1003 770
1-Methylenecyclohexene-1	109-109.2 (760mm)	1.4508	0.8134	1676	—	—
Vinylcyclohexane	125 (740 mm)	1.4470	0.8091	1641	—	—
Catalyzate VII (After passing 1-ethylcyclohexene-1 over the contact catalyst)	131-134 (757 mm)	1.4568	0.8170	1641 1653 1671	Starting vinylcyclohexane ∼3% 1-Ethylcyclohexene-1 ∼75% 1-Ethylcyclohexene-2 ∼13% Ethyl benzene∼3.0% Ethyl cyclohexane∼6.0%	1641 1671 1653 1003 —
1-Ethylcyclohexene-1	135.2-135.5 (768mm)	1.4562	0.8159	1671	—	—
Catalyzate VIII (After passing 1-ethylcyclohexene-1 over the contact catalyst)	133 -135 (760 mm)	1.4564	0.8182	1651 1671	Recovered 1-ethylcyclohexene-1∼78% 1-Ethylcyclohexene-2∼17% Ethylbenzene∼2% Ethylcyclohexane∼4%	1671 1651 1004 —
1-Ethylcyclohexene-2	131.7-132.0 (760mm)	1.4500	0.8104	1651	—	—
Catalyzate IX (After passing 1-ethylcyclohexene-2 over the contact catalyst)	132.0-134.5 (758mm)	1.4547	0.8178	1650 1671	Recovered 1-ethylcyclohexene-2∼25% 1-Ethylcyclohexene-1 ∼50% Ethylbenzene∼8.0% Ethylcyclohexane∼17%	1650 1671 1003 —
Allylcyclohexane	151.2-151.5 (757mm)	1.4500	0.8135	1641	—	—
Catalyzate X (After passing allylcyclohexane over the contact catalyst)	152 -154 (752 mm)	1.4552	0.8221	1641 1653 1671	Recovered allylcyclohexane∼15% 1-Propylcyclohexene-1 ∼79%*** 1-Propylcyclohexene-2 ∼2% Propylbenzene∼2% Propylcyclohexane∼4%	1641 1671 1653 1001 —
1-Propylcyclohexene-1	153.5-154 (750 mm)	1.4573	0.8279	1670	—	—

Notes for Table 2

* By analogy with the characteristic frequency of 1-ethylcyclohexene-2.

** Because there is a characteristic frequency at 1651 cm^{-1} in the Raman spectrum of the starting methylenecyclohexane, the presence of this frequency in the spectrum of catalyzate VI could be attributed to the presence of

(Notes continued on the top of p. 586).

TABLE 3

Hydrocarbons and catalyzates	Boiling point	n_D^{20}	d_4^{20}	Characteristic frequency of the C=C bond in the Raman spectrum cm^{-1}	Composition of the catalyzate	Notes
Methylene cyclopentane	73-73.2 (750 mm)	1.4342	0.7803	1653	–	–
Catalyzate I (after passing methylene cyclopentane over the contact catalyst)	73.2-74.5 (749 mm)	1.4314	0.7781	1657	1-Methylcyclopentene-1 (without contamination from the starting methylenecyclopentane)	Established by the complete set of frequencies in the spectrum and the absence of the frequency of the starting material
1-Methylencyclopentene-1	74.3-74.4 (747 mm)	1.4326	0.7765	1657	–	–
Vinylcyclopentane	98.5-98.7 (762 mm)	1.4375	0.7834	1641	–	–
Catalyzate II (after passing vinylcyclopentane over the contact catalyst)	106-107 (773 mm)	1.4420	0.8001	1654	1-Ethylcyclopentene-1 (with contamination from the starting vinyl cyclopentane)	Established by the complete set of frequencies in the spectrum and the absence of the frequency of the starting hydrocarbon
1-Ethylcyclopentene-1	105 (760mm)	1.4444	0.8015	1653	–	–
Catalyzate III (after passing 1-ethylcyclopentene-1 over the contact catalyst)	105-106 (757 mm)	1.4440	0.8024	1653	Starting 1-ethylcyclopentene-1	The spectrum of the catalyzate was identical to that of the starting hydrocarbon.
1-Ethylcyclopentene-2	96.7-96.8 (750 mm)	1.4319	0.7835	1617	–	–
Catalyzate IV (after passing 1-ethylcyclopentene-2 over the contact catalyst)	98-102 (761 mm)	1.4370	0.7904	1617	Starting 1-ethylcyclopentene-2 ~60%	Determined by the line 1617 cm^{-1}
				1653	1-Ethylcyclopentene-1 ~40%	Determined by the line 1653 cm^{-1}
Allylcyclopentane	124-124.5 (756 mm)	1.4400	0.7912	1641	–	–
Catalyzate V (after a single pass of allylcyclopentane over the contact catalyst)	129.5-130 (760 mm)	1.4468	0.7943	1641	Starting allylcyclopentane ~33%	Determined by the line 1641 cm^{-1}
				1653	1-Propylcyclopentene-1 ~30%	Determined by the line 1653 cm^{-1}
				1672	Trans-propenylcyclopentane ~36%	Determined by the line 1672 cm^{-1} *
Catalyzate Va (after two passes of allylcyclopentane over the contact catalyst)	129-130 (758 mm)	1.4446	0.7952	1653	1-Propylcyclopentene-1 ~57%	Determined by the line 1653 cm^{-1}
				1672	Trans-propenylcyclopentane ~43%	Determined by the line 1672 cm^{-1} *
1-Propylcyclopentene-1	129.5-130 (752 mm)	1.4430	0.7959	1653	–	–

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* Characteristic for transalkenes.

Notes for Table 2 (continued)

unchanged (under these isomerization conditions) methylene cyclohexane; however, other sufficiently intense lines of this hydrocarbon were absent in the spectrum of the catalyzate: (309 cm^{-1}; 406 cm^{-1}; 842 cm^{-1}; 899 cm^{-1}; 1103 cm^{-1}; 1144 cm^{-1}; 1250 cm^{-1}; 1320 cm^{-1}; 1684 cm^{-1} [9]. Therefore, the appearance of the frequency 1651 cm^{-1} in catalyzate VI could be caused only by the presence of 1-methylcyclohexene-2 (with a possible contamination with 1-methylcyclohexene-3), since the frequency 1651 cm^{-1} is characteristic for 1-alkylcyclohexenes-2 [9].

*** An intense frequency, 1671 cm^{-1} which was used for the calculation of the amount of 1-propylcyclohexene-1 in catalyzate X, is characteristic not only for 1-alkylcyclohexenes-1, but also for the trans form of the disubstituted ethylene. Upon the isomerization of ethylcyclohexene, a hydrocarbon of this type of structure could have been formed in catalyzate X, trans-propenylcyclohexene, however, apparently, this hydrocarbon was absent in catalyzate X (or its amount was negligible) because the ratio of the intensity of the lines 1670 and 748 cm^{-1} was found in essence to be identical in the free 1-propylcyclohexene-1 and in the catalyzate X.

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photometrically by the analytical lines of the spectra of the catalyzate for which, with the aid of the corresponding curves for the extinction, the intensity was calculated; for the calculation of the percent composition of the component, photometric data on the intensity of the lines in the spectra of the individual hydrocarbons (in a unit objective scale — $I\dot{\omega}$ per mole and cm^{-1}) was used.

The differential intensity $I\dot{\omega}$ per mole and cm^{-1} were obtained with a 6 cm^{-1} slit on the spectrum and were expressed on a unit scale in which the differential intensity of the line 801 cm^{-1} of cyclohexane was adopted for 250 units per mole and cm^{-1}.

Upon the measurement of the intensity of the line in the region of 1640-80 cm^{-1}, in the Raman spectrum of the hydrocarbons studied, a constant intensity of a characteristic frequency for a C=C, was established, namely, the differential intensity (per mole and cm^{-1}) equal to 115-130 [12].

The determination of the cyclohexane hydrocarbons (product of the irreversible catalysis) in the catalyzates VI, VII, VIII, IX, and X was difficult because of the overlapping of their more intense lines by the lines of the starting and resulting hydrocarbons; for this reason the amount of methyl-, ethyl-, and propylcyclohexane in these catalyzates was calculated from the amount of aromatic hydrocarbons found (the ratio of the amount of the cyclohexane to the aromatic hydrocarbons was taken to be equal to 2:1, according to the scheme of irreversible catalysis.)

Conclusions on the composition of the catalyzate made on the basis of the spectroscopic data are given in Tables 2 and 3.

In order for such amounts of products of the irreversible catalysis to be formed in catalyzates VI, VII, and X, obtained by the isomerization of methylene, vinyl, and allylcyclohexane, from which cyclohexane hydrocarbons could be separated and characterized by constants, they were passed repeatedly over the contact catalyst under the following conditions: 20 ml of each newly obtained catalyzate was treated with sulfuric acid in order to remove the unsaturated and aromatic hydrocarbons (80%, 96%, and fuming sulfuric acid with 7% SO_3). In each case, the cyclohexane hydrocarbons which did not react with the sulfuric acid, 2.8, 3.0, and 4.4 ml of methyl, ethyl, and propylcyclohexane, respectively, were washed to neutrality, dried with calcium chloride, and distilled over sodium. The constants of the cyclohexane hydrocarbons agreed with those in the literature.

SUMMARY

1. The contact isomerization of unsaturated five and six membered cyclic hydrocarbons (with a double bond in side chain and in the ring) proceeding with a rearrangement of the double bond, was studied.

2. It was shown that, upon the passage of alkenylcyclopentanes over chromic oxide on aluminum oxide at 250°, the double bond rearranged from the side chain into the ring and remained at the alkylated carbon atom of the ring. Methylene and vinyl cyclopentane were completely transformed into the corresponding 1-alkylcyclopentene-1; for the example of allylcyclopentane, a hydrocarbon with a double bond farther away from the ring, the presence of one of the intermediate products of the sequence rearrangement of the side chain double bond (transpropenylcyclopentane) (in addition to 1-propylcyclopentene) could be shown.

3. It was shown that alkenylcyclohexanes (methylene, vinyl and allylcyclohexanes) resembled the alkenylcyclopentanes, and isomerized by the rearrangement of the double bond from the side chain into the ring on passing them over chromic oxide on aluminum oxide at 250°, to form the corresponding 1-alkylcyclohexenes-1 as the main products; the 1-alkylcyclohexenes-1 formed rearranged partially into the 1-alkylcyclohexenes-2 (with possible contamination of 1-alkylcyclohexenes-3) under these conditions.

4. It was shown that 1-alkylcycloalkenes-2 (1-ethylcyclopentene-2 and 1-ethylcyclohexene-2) were isomerized on passing them over chromic oxide on aluminum oxide at 250° by 40-50% into 1-aklylcycloalkenes-1 (1-ethylcyclopentene-1 and 1-ethylcyclohexene-1, respectively); the double bond migrated from the ring to the alkylated carbon atom.

5. It was shown that 1-alkylcyclopentenes-1 and 1-alkylcyclohexenes-1 were considerably more stable to isomerizing action of the contact catalyst, chromic oxide on aluminum oxide (at 250°), than the isomeric 1-alkylcycloalkenes-2.

6. It was shown that 1-alkylcyclohexenes with different position for the double bond in the ring, formed during the isomerization (over chromic oxide on aluminum oxide at 250°) of all of the investigated six membered cyclic hydrocarbons, underwent a small degree of irreversible catalysis, transforming into a mixture of the corresponding alkylbenzene and alkylcyclohexane.

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* See Consultants Bureau translation, p. 727.

REACTIONS OF ALDEHYDES AND KETONES WITH ACETIC ANHYDRIDE

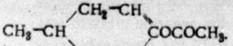
II. PREPARATION OF ENOL ACETATES AND DIACETATES OF THE HYDRATED FORM OF 4-METHYL- AND 4-TERT-BUTYLCYCLOHEXANONE

I. V. Machinskaya

In the previous communication [1], it was shown that, by the action of acetic anhydride on cyclohexanone in the presence of small amounts of sulfuric acid and at room temperature, the formation of cyclohexanone enol acetate, as well as the diacetate of the dihydrated form of cyclohexanone, occurred. During the investigation, experimental results were obtained which led to the conclusion that the formation of the enol acetate of cyclohexanone occurred by means of an intermediate stage of the formation of the diacetyl compound which decomposed into acetic acid and the enol acetate under the reaction conditions. The aim of the present study was to investigate the reaction of acetic anhydride with homologs of cyclohexanone under these conditions 4-methyl- and 4-tert.-butylcyclohexanone.

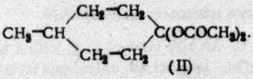
The reaction between 4-methylcyclohexanone and acetic anhydride was previously studied by Mannich and Hanen [2] who conducted it in the presence of sodium acetate and obtained 4-methylcyclohexenyl-Δ_1 acetate. This compound was also obtained by Grignard and Mingasson [3] by the partial hydrogenation of p-cresol and the subsequent introduction of the reaction product into a boiling mixture of acetic anhydride and sodium acetate.

It was shown that, by the reaction of cyclohexanone with acetic anhydride in the presence of a small amount of sulfuric acid at room temperature for 42 hours, the main reaction product was also 4-methylcyclohexenyl-Δ_1-acetate (I).

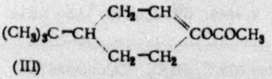

(I)

After a 42-hour reaction, the yield of the crude product with b.p. 50-60° at 3 mm was about 70% of the theoretical.

With a shorter reaction of 4-methylcyclohexanone with acetic anhydride (9 hours) in the presence of H_2SO_4, in addition to 4-methylcyclohexenyl acetate, an oily substance with an ethereal odor, b.p. 90-90.5° at 3 mm, was obtained. The results of the elementary analysis corresponded to the formula $C_{11}H_{18}O_4$, which is that of 4-methylcyclohexylidene diacetate, previously unreported in the literature (II). The molecular refraction and saponification number upheld this formula.


(II)

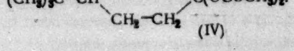
As a result of the reaction of 4-tert-butylcyclohexanone with acetic anhydride in the presence of small quantitites of sulfuric acid at room temperature for 9 days, two substances were obtained: 1) an oily product with b.p. 87° at 3 mm. The elementary analytical results corresponded to the formula $C_{12}H_{20}O_2$, which was that of 4-tert.-butylcyclohexenyl-Δ_1-acetate (III).


(III)

The molecular refraction and saponification number of the product obtained also corresponded to the calculated for this compound.

2) A colorless crystalline product with an m.p. 48-50°, which gave a considerable depression in m.p. when mixed with the starting substance. The results of the elementary analysis and the saponification number of the compound obtained showed that it was the diacetate of the hydrated form of 4-tert.-butylcyclohexanone, 4-tert.-butylcyclohexylidene diacetate (IV).

4-Tert.-butylcyclohexenyl-Δ_1-acetate and 4-tert.-butylcyclohexylidene diacetate have not been reported in the literature.


(IV)

On the basis of the results obtained, it can be concluded that 4-methyl- and 4-tert.-butylcyclohexanone reacted with acetic anhydride in the presence of sulfuric acid, analogously to cyclohexanone, to give the enol acetate and diacetyl derivative of the hydrated form of the ketone with a short reaction period; with a prolonged reaction time, the diacetyl compound was not obtained; only the enol acetate formed. If it is assumed that, in the given case, as in the case of cyclohexanone, the reaction proceeds by means of the intermediate formation of the diacetate, it can be concluded that the presence of a methyl group in position 4 of the cyclohexanone ring, accelerates the reaction of the transformation of the diacetate into the enol acetate. Thus, in the case of the unsubstituted cyclohexanone, the diacetate and monoacetate were obtained after 24 hours of reaction; with 4-methylcyclohexanone, only the monoacetate was obtained with this reaction time. On the other hand, the presence of the 4-tert.-butyl group, evidently, has a decelerating effect on the decomposition of the diacetate. Thus, in the case of the unsubstituted cyclohexanones, by prolonging the reaction for 9 days, the corresponding diacetate could not be isolated; with tert.-butylcyclohexanone, a small amount of the diacetate was obtained for the same reaction time.

The great instability of the products of the addition of acetic anhydride to 4-methyl and 4-tert.-butylcyclohexanone must be mentioned; they decompose with the formation of lower boiling products upon vacuum distillation at pressures greater than 4-5 mm, as well as upon the distillation of large amounts even at pressures of 3 mm. In relation to the enol acetate of cyclohexanone, as well as those of its homologs, it must be mentioned that they distill at a wide temperature interval, possibly, because they are mixtures of cis and trans isomers.

EXPERIMENTAL

The starting ketones, 4-methyl- and 4-tert. butylcyclohexanone were obtained from the corresponding 4-alkylcyclohexanols by oxidation with chromic mixture; 4-methylcyclohexanone was purified by the preparation of the bisulfite compound. The yield of 4-methylcyclohexanone, purified by means of the bisulfite compound, was 59% of the theoretical calculated on the alcohol reacted; the yield of 4-tert.-butylcyclohexanone was 60% of the theoretical.

I. Reaction of 4 Methylcyclohexanone with Acetic Anhydride. 0.32 ml of concentrated sulfuric acid was added rapidly dropwise to a mixture of 44.4 g (0.4 mole) of 4-methylcyclohexanone (b. p. 167-170°) and 124 g (1.2 moles) of acetic anhydride (b. p. 137-140°). A spontaneous heating up to 32° occurred, the reaction mixture gradually acquired a red brown color. After 9 hours of standing at room temperature, the reaction mixture was treated with a mixture of ice and water to decompose the unreacted acetic anhydride until the lower oily layer did not float up. The reaction product was extracted with ether. The water layer was neutralized with sodium carbonate and once more extracted with ether, the combined ether extracts were washed with 10% sodium carbonate solution. The unreacted ketone was extracted from the ether solution with bisulfite; weight of the bisulfite compound, 44.5 g, which corresponds to 23 g of methylcyclohexanone. After washing the ether extract with sodium carbonate solution and water, it was dried with sodium sulfate and the ether removed. The residue was vacuum distilled several times; two substances were isolated.

1) An oily product (5 g) with a weak ethereal odor; b. p. 191-193°, b. p. 53-56° at 3 mm; n_D^{23} 1.4520; d^{20} 0.9797; MR_D 42.46; calculated for methylcyclohexenyl acetate, 42.75.

Found %: C 69.44; H 9.46; saponification number 356. $C_9H_{14}O_2$. Calculated %: C 70.90; H 9.15, saponification number 364.

2) A small amount of an oilyproduct with a b. p. 90-90.5° at 3 mm; n_D^{20} 1.4443; d^{20} 1.05179, MR_D 54.14; calc. for methylcyclohexylidene diacetate, 54.11.

Found %: C 61.3, 61.71, 61.36; H 8.61, 8.9, 8.67; saponification number 512. $C_{11}H_{18}O_4$. Calculated %: C 61.66; H 8.49; saponification number 524.

II. Reaction of 4-Tert. - butylcyclohexanone with Acetic Anhydride. 0.16 ml of sulfuric acid was added to a solution of 30.8 g (0.2 mole) of 4-tert. - butylcyclohexanone (m. p. 49°) in 62 g (0.6 mole) of acetic anhydride (b. p. 137-140°). A small amount of heat was evolved spontaneously; the mixture gradually became a red brown color. After 9 days of standing at room temperature, the mixture was treated as in experiment I. The treatment with bisulfite was not done since 4-tert. - butylcyclohexanone in ether solution did not give a crystalline condensation product with bisulfite.

After many vacuum distillations of the residue, after the removal of the solvent, two products were isolated: 1) a liquid with an ethereal odor, b. p. 87° at 3 mm; n_D^{20} 1.4641; d^{20} 0.9593; MR_D 56.47; calc. for tert.-butylcyclohexenyl acetate, 56.60.

Found %: C 73.55, 73.40; H 10.46, 10.54; saponification number 273. $C_{12}H_{20}O_2$. Calculated %: C 73.42; H 10.27; saponification number 286.

2) The second product had a b. p. 113-115° at 3 mm; on standing crystals separated which, after recrystallization from slightly warmed ethyl alcohol, had a m. p. 49-51°. A mixed melting point with the starting ketone gave a large depression.

Found %: C 66.17; H 9.73; saponification number 428. $C_{14}H_{24}O_4$. Calculated %: C 65.60, H 9.44; saponification number 438.

SUMMARY

The reaction of 4-methyl and 4-tert.-butylcyclohexanone with acetic anhydride in the presence of a small amount of sulfuric acid was studied at room temperatures. It was found that, with a short reaction time of these cyclohexanone homologs with acetic anhydride, the corresponding enol acetates, in addition to the diacetates of the hydrated form of the ketone were obtained; on more prolonged reaction, the diacetate compound was not obtained; only the enol acetate was formed.

4-tert. -butylcyclohexanone enol acetate, 4-tert. -butylcyclohexenyl-Δ_1-acetate, as well as the diacetate of the hydrated forms of both ketones, 4-methylcyclohexylidene diacetate, and 4-tertiary-butylcyclohexylidene diacetate have not been described in the literature.

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* See Consultants Bureau Translation, p. 1205.

THE QUESTION OF METHODS FOR THE DETERMINATION OF THE STRUCTURE OF TERTIARY ACETYLENIC ALCOHOLS AND γ-ACETYLENIC GLYCOLS

A. I. Lebedeva and T. A. Mishnina

In spite of the large number of papers on the question of the determination of the structure of acetylenic compounds, up to now there is no convenient and successful method which can be used to characterize this class of hydroxy derivatives of acetylene. Oxidation and ozonation methods are frequently employed to determine the structure of unsaturated compounds, oxidation of the acetylenic compounds ordinarily being used, like the oxidation of compounds of the ethylene series. However, even E. E. Wagner [1] stated that variations in this scheme were possible, which were suggested and confirmed by a subsequent series of investigations.

From the large amount of papers on the oxidation of acetylenic alcohols and glycols by aqueous solutions of potassium permanganate the following conclusions were drawn: that hydroxy acids are always formed initially, which are then further oxidized, as a result of which the yield of these substances diminishes greatly, and even becomes zero. However, such a conclusion is not, apparently, completely correct. It must be remembered that, alongside the oxidation of the primary reaction products – the hydroxy acids – the yeild of the latter is also decreased as the result of the parallel oxidation processes so that no hydroxy acids are produced at all.

Dupont [2] first showed that, upon the oxidation of acetylenic γ-glycols by an aqueous potassium permanganate solution, the reaction can proceed simultaneously in two directions:

$$\begin{array}{l} \mathrm{R(R_1)COH-C{\equiv}C-COH(R_1)R} + 2\mathrm{KMnO_4} \rightarrow 2\mathrm{R(R_1)COH-COOH} \qquad \text{(I)} \\ \qquad\qquad\quad\downarrow \\ \qquad 2\mathrm{RCOR_1} + \mathrm{HOOC-COOH} \qquad \text{(II)} \end{array}$$

The second direction, as Du Pont showed, sometimes predominates. For this reason, in order to increase the yields of the hydroxy acid, he proposed that the ethers or esters of the glycol be oxidized. Krestinsky [3] investigated the oxidation of tetramethylbutyndiol by potassium permanganate in detail and confirmed Du Pont's results. Later Lvov and co-workers [4] studied the decomposition of tetramethylbutyndiol with various oxidizing agents in order to increase the yield of the α-hydroxyisobutyric acid and came to the conclusion that the primary reaction product is α-hydroxyisobutyric acid alone, which partly oxidizes during the conditions of the experiment, forming acetone and carbon dioxide.

During attempts to find a more successful method for the structure determination of acetylenic alcohols, glycols, and diacetylenic glycols, the solution of the problem of whether ketones and oxalic acid are formed as a result of a secondary reaction, as suggested by many investigators, or by means of the oxidation occurring in two directions as suggested by Du Pont, was attempted; in addition an attempt was made to see whether or not there was a definite relationship between the structure of the compound used and the direction of the reaction. As starting materials, acetylenic alcohols of the general formula: $\mathrm{R(R_1)COH-C{\equiv}CH}$ and γ-acetylenic glycols of the general formula:

$$\mathrm{R(R_1)COH-C{\equiv}C-COH(R_1)R}$$

were used.

In both cases, a hydroxy acid should be formed by the oxidation by means of the first scheme. If this hydroxy acid would be oxidized further, then, independent of the fact that acetylenic alcohols or the corresponding acetylenic glycols were being used, the amount of the hydroxy acid formed during the oxidation should be approximately the same in both cases.

However, as is apparent from Table 1, upon the oxidation of dimethylacetylenylcarbinol an insignificant amount of acetone was obtained, and not even a trace of oxalic acid could be detected qualitatively. The α-hydroxyisobutyric acid yield was 80% of the theoretical, whereas Krestinsky obtained a large amount of acetone, 63% of oxalic acid, and 18% of α-hydroxyisobutyric acid. Lvov and co-workers tried by every means to increase the yield of α-hydroxyisobutyric acid during the oxidation of tetramethylbutyndiol, but were not successful. If it is assumed that the primary reaction product in both cases is α-hydroxyisobutyric acid, then it becomes incomprehensible why it does not oxidize further in the case of dimethylacetylenyl carbinol, whereas with tetramethylbutyndiol it does. This same phenomenon was found with the following pairs of compounds investigated: namely, during the oxidation of methyl-p-tolylacetylenylcarbinol only 2.6% of oxalic acid and 37.0% of p-tolyllactic acid were isolated. Upon the oxidation of symm.-dimethyldi-p-tolylbutyndiol, 15% of oxalic acid and about 16% of p-tolyllactic acid were obtained. From the Table it is apparent that the main reaction direction for tertiary acetylenic alcohols is usually the first, while for acetylenic γ-glycols, the reaction direction depends mainly on the structure of the glycols oxidized. It is difficult to compare these results with those obtained by Krestinsky, but in the case of the glycols oxidized by the authors, it can be stated that the yield of the products formed by the oxidation according to the second scheme, evidently, increased with increase in the molecular weight of the radicals, and especially upon going from aliphatic radicals to aromatic.

Therefore, if a necessity for structure determination of hydroxy derivatives of acetylene by means of oxidation with potassium permanganate in aqueous or acetone solution arises, then such a determination can be recommended only for acetylenic alcohols, and then only with a quantitative separation of the neutral and acidic products. The method is not very applicable to the determination of the structure of diacetylenic glycols of the general formula:

$$R(R_1)COH-C\equiv C-C\equiv C-COH(R_1)R.$$

EXPERIMENTAL

In all experiments on oxidations, attempts were made to stay within the conditions given by Du Pont. For the oxidation of symm.-dimethyl-p-tolylbutyndiol and tetra-p-tolylbutyndiol, acetone instead of water was used as the solvent because these compounds did not react with potassium permanganate in water.

Oxidations with Potassium Permanganate in Water. The quantity of the substance shown in Table 1 was used for each experiment. The compound to be oxidized was dissolved, or stirred strongly until it was emulsified, in one hundred volumes of water. To the solution or emulsion so obtained, cooled externally by water and ice and mixed efficiently, the calculated amount of finely pulverized potassium permanganate was added slowly in small portions. All of the potassium permanganate was added within several hours. The solution was left to stand overnight, the manganese dioxide was filtered, and thoroughly washed several times with boiling water. The wash water was added to the filtrate.

For oxidation of compounds with aliphatic radicals, the neutral products were steam distilled into a solution of p-nitrophenylhydrazine acetate. For oxidations of dimethylacetylenylcarbinol and diethylacetylenylcarbinol, such small precipitates of the corresponding p-nitrophenylhydrazones were obtained that it was even difficult to recrystallize them. For the oxidation of compounds with arylaliphatic radicals the neutral products were extracted with ether. After the removal of the ether, the residue was distilled or crystallized and then identified.

The characteristic neutral products and the derivatives obtained from them are given in Table 2.

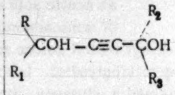
The solution remaining after the removal of the neutral products was evaporated to a small volume, and acidified with the calculated amount of sulfuric acid (1:1). The hydroxy acids were extracted by hand with ether, and after the removal of the ether, were recrystallized or distilled.

α-Hydroxyisobutyric acid was recrystallized from benzene, α-hydroxyethylacetic acid was purified by distillation. p-Tolyllactic acid recrystallized from a mixture of petroleum ether and benzene, had a m. p. 107-108°. In the literature reference, a m. p. 101-102° [5] and 102-104° [6] was found for p-tolyllactic acid; for this reason, the equivalent for the acid obtained was determined and an analysis was made of the silver salt for the percent silver; the results given in Table 3, correspond to those for p-tolyllactic acid.

The acidic solution remaining after extraction by hand, was extracted continuously for a prolonged time (about a week) in a percolator with ether. From the mixture obtained after the extraction, consisting of a small amount of a hydroxy acid and oxalic acid, the oxalic acid was precipitated in the form of the calcium salts.

Oxidations with Potassium Permanganate in Acetone. The amount of the substance used is given in Table 1. The compound to be oxidized was dissolved in 25 parts by weight of acetone, and the calculated

TABLE 1

Expt. No.	Name of Compound	Amount of compound used for oxidation (g)	Neutral products obtained after oxidation (g)	(%)	Hydroxyacids obtained after the oxidation (g)	(%)	Amount of oxalic acid (g)	(%)	Notes
	Alcohols $R(R_1)COH-C\equiv CH$ (general formula)								
1	Dimethylacetylenyl-carbinol $R=R_1=CH_3$	5	Acetone – traces		α-Hydroxyisobutyric 5.0	80.8	None	None	
2	Diethylacetylenyl-carbinol $R=R_1=C_2H_5$	8	Diethylketone – traces		α-Hydroxyethylacetic 5.0	53.0	0.25	4.0	
3	Methyl-p-tolylacetyl-enylcarbinol $R=CH_3$; $R_1=C_7H_7$-n	6	Methyl-p-tolyl ketone 1.1	21.6	p-Tolylacetic 2.5	37.0	0.09	2.6	
	Glycols  (general formula)								
4	Tetramethylbutyndiol* $R=R_1=R_2=R_3=CH_3$	15	Acetone-not found		α-Hydroxyisobutyric 4.0	18.1		63.1	
5	Symm.-dimethyl-p-tolylbutyndiol $R=R_2=CH_3$ $R_1=R_3=C_7H_7$-n	9	Methyl-p-tolyl ketone 3.8	62.5	p-Tolyllactic 1.3	15.9	0.31	15.3	The oxidation was conducted in acetone. 2.3 g of the starting glycol was recovered.
6	Tetra-p-tolylbutyndiol $R=R_1=R_2=R_3=C_7H_7$-n	8	Di-p-tolyl ketone 3.2	50.7	Di-p-tolylglycolic 0.8	12.2	0.32	28.4	2.3 g of the starting glycol was recovered. The oxidation was conducted in acetone.

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* The oxidation of tetramethylbutyndiol was conducted by V. N. Krestinsky [3].

TABLE 2

Expt. No.	Name of compound	Temperature		Derivatives obtained	M.p. of the derivatives obtained
		Boiling	Melting		
1	Acetone	–	–	p-Nitrophenylhydrazone	146-147°
2	Diethylketone.	–	–	p-Nitrophenylhydrazone	139-141
3	Methyl-p-tolyl ketone.	92-94° (7 mm)	–	Semicarbazone	204-205
4	Di-p-tolyl ketone . . .	–	94-96°	–	–

TABLE 3

Expt. No.	Name of compound	Melting point	Acid equivalent		Analysis of silver salt	
					silver	
			Found	Calc.	Found	Calc.
1	α-Hydroxyethylacetic acid.	73-75°	–	–	–	–
2	p-Tolyllactic.	107-108	180.5	180.1	37.61	37.58
3	Di-p-tolylglycolic	129-130	256.6	256.3	29.92	29.78

amount of finely pulverized potassium permanganate was added gradually in small portions with external cooling by ice and water, and with efficient mixing. On the following day, the acetone solution was filtered from the manganese dioxide. The latter was washed several times with acetone, and the wash acetone was combined with the main solution. In the case of symm-di-p-tolylbutyndiol, the substance was distilled at 92-94° (7 mm) after the removal of the acetone. The product gave a precipitate with an acetic acid solution of semicarbazide. The semicarbazone had a m.p. 204-205° which corresponded to the melting point of methyl p-tolyl ketone semicarbazone. The crystalline residue in the flask was found to be the starting dimethyl-p-tolylbutyndiol. In the case of tetra-p-tolylbutyndiol, after the removal of the acetone, in the flask there remained a substance with m.p. 77-87°. After many recrystallizations from alcohol, one product with m.p. 94-96°, which did not give a depression with di-p-tolyl ketone, and another product with m.p. 153-154°, not giving a depression with tetra-p-tolylbutyndiol, were obtained. In order to determine the amount of ketone and starting glycol, the mixture of the neutral products was catalytically hydrogenated in the presence of platinum. Only 45% of hydrogen was combined (if it is considered that the entire mixture was the starting acetylenic glycol). In this way it was possible to determine the amount of di-p-tolylbutyndiol in the mixture of neutral products obtained.

For the separation of the acidic products, the manganese dioxide residue was boiled with water and filtered. The filtrate was evaporated to a small volume, and acidified with the calculated amount of sulfuric acid; the acidic products were then processed in the same manner as for the oxidation with an aqueous solution of potassium permanganate. The acid obtained by the oxidation of tetra-p-tolylbutyndiol, di-p-tolylglycolic acid, melted at 129-130°, after recrystallization from water. An m.p. 135° [7] is given for this acid, for this reason the equivalent of the acid obtained was determined, and an analysis of its silver salt was made; the results, given in Table 3, corresponded to those for di-p-tolylglycolic acid.

SUMMARY

1. Upon the oxidation of tertiary aliphatic acetylenic alcohols of the general formula $R(R_1)COH-C\equiv CH$ by aqueous potassium permanganate solutions, α-hydroxy acids were formed mainly, in addition to small amounts of the ketone, and oxalic acid. The method can be used for structure determination of such alcohols, and for the synthesis of their α-hydroxy acids.

2. During the oxidation of di-tertiary acetylenic glycols with potassium permanganate in water or acetone solution, the reaction proceeds in the direction of the formation of hydroxy acids, as well as in the direction of the

formation of ketones and oxalic acid, i.e. these products are formed which should be obtained during the oxidation of ditertiary diacetylenic glycols. The yields of these products depend on the character of the radicals entering into the composition of the given glycol, for this reason the method cannot be recommended for structure determination of acetylenic and diacetylenic glycols, nor for the synthesis of the corresponding hydroxy acids from the acetylenic glycols.

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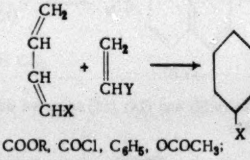
DERIVATIVES OF ACETYLENE. 153.

DIENIC CONDENSATION OF 1-VINYL-Δ^1-CYCLOHEXENE WITH METHACRYLIC ACID, METHYL METHACRYLATE, ACROLEIN, β,β-DIMETHYLDIVINYL KETONE, AND CROTONIC ACID

I. N. Nazarov and T. D. Nagibina

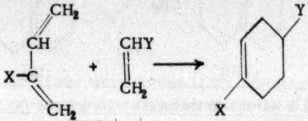
In spite of the large number of papers on the study of the dienic reaction syntheses, the question of the structure of the condensation products of α,β-substituted dienes and asymm. derivatives of ethylene has scarcely been investigated up to now. It is known that α-substituted dienes form the so-called "ortho" substituted cyclohexenes (I) [1,2,3,4] upon reaction with asymm. dienophiles:



(I)

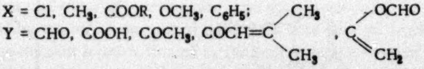
X = CH_3, CN, COOH, COOR, COCl, C_6H_5, $OCOCH_3$;
Y = CHO, $COCH_3N$, COOH, COCl, CH = CH_2.

The analogous condensation with β-substituted dienes gives the "para" substituted cyclohexenes (II) [5,6,7] mainly:



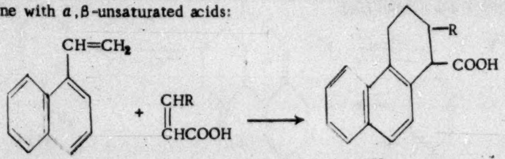
(II)

X = Cl, CH_3, COOR, OCH_3, C_6H_5;



$$Y = CHO,\ COOH,\ COCH_3,\ COCH{=}C\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix},\ C\begin{smallmatrix}OCHO\\=CH_2\end{smallmatrix}$$

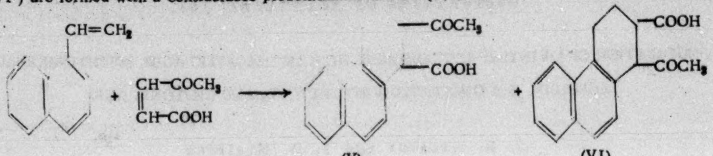
It was of great interest also to study the order of addition of asymm. dienophiles to α,β-substituted dienes. The cyclic dienes of the type 1-vinyl-Δ^1-cyclohexene, 1-vinylnaphthalene, 1-vinyl-3,4-dihydronaphthalene, and 1-vinyl-Δ^1-octalin can be assigned to the latter group. Dienic condensations with the participation of cyclic dienes of the type 1-vinyl-3,4-dihydronaphthalene and 1-vinyl-Δ^1-octalin are also of considerable interest because these reactions are applied for the synthesis of substances related to the steroids [8]. Recently, it was shown that only 1-substituted acids of the hydrophenanthrene series (IV) [9] are formed by the condensation of 1-vinylnaphthalene with α,β-unsaturated acids:



(III) (IV)

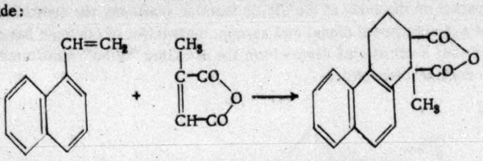
R = CH_3, C_2H_5

In the case of the condensation of 1-vinylnaphthalene with β-acetylacrylic acid, two isomeric acids (V) and (VI) are formed with a considerable predominance of acid (V) [10]:



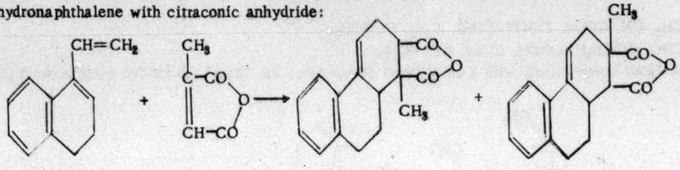
(V) (VI)

Only the anhydride (VII) [11] was separated from the reaction of 1-vinylnaphthalene with citraconic anhydride:



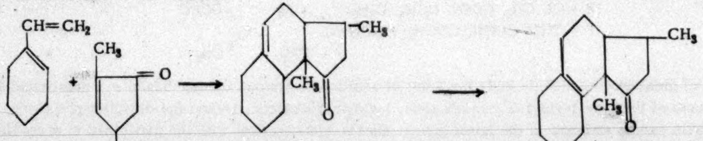
(VII)

The formation of two isomeric anhydrides (VIII) and (IX) [12] occurred during the condensation of 1-vinyl-3,4-dihydronaphthalene with citraconic anhydride:



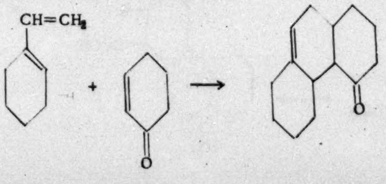
(VIII) (IX)

In the previous communication [13] it was shown that a tricyclic ketone (X) is formed by the condensation of 1-vinyl-Δ^1-cyclohexene with 1,3-dimethyl-Δ^1-cyclopentene-5-one, which isomerized partly into the ketone (XI) under the conditions of the reaction:

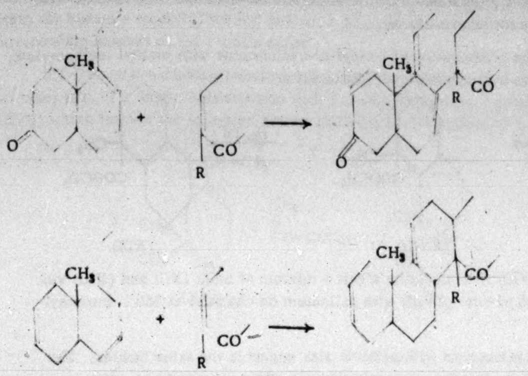


(X) (XI)

By the condensation of 1-vinyl-Δ^1-cyclohexene with Δ^1-cyclohexene a ketone of the hydrophenanthrene series containing a carbonyl in position 4 was formed [14]:

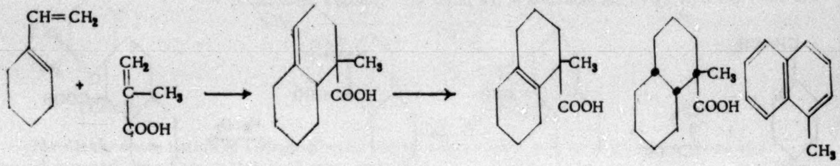


As it was shown with many examples in the authors' laboratory, vinyl dienes of the type 1-vinyl-Δ^1-octalene condense in the same way as α,β-unsaturated bicyclic ketones. These condensations lead to the formation of unsaturated steroidal ketones with the so-called "inverted" structure (the carbonyl group in the steroidal skeleton is found in position 15 and not in 17 as in the "normal" steroids) [15]:



R = H or CH_3

It was of interest to study the dienic condensation reaction of 1-vinyl-Δ^1-cyclohexene also with the simpler asymm. dienophiles, for which methacrylic acid, methyl methacrylate, acrolein, β,β-dimethyldivinyl ketone, and crotonic acid were chosen. It was found that a mixture of acids (XII) and (XIII) were formed by heating 1-vinyl-Δ^1-cyclohexene with methacrylic acid at 135-140° for 8 hours. By the dehydrogenation of acid (XII) with Raney Ni in benzene at 380-390°, α-methylnaphthalene (XIV) was obtained:

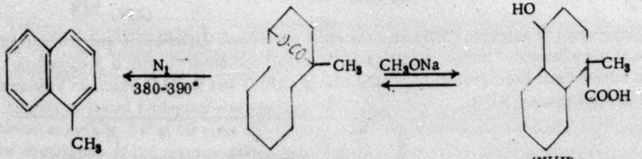


(XII) (XIII) (XV) (XIV)

A small amount of naphthalene was detected in the dehydrogenation products of acids (XII) and (XIII), which was formed as a result of the cleavage of the methyl group as well as the carboxyl.

In spite of careful search of the dehydrogenation products, 2-methylnaphthalene could not be isolated, and therefore the condensation of 1-vinyl-Δ^1-cyclohexene goes only in one direction to form the crystaline acid (XII) which isomerizes partly by the rearrangement of the double bond into the liquid acid (XIII). A mixture of stereoisomeric acids of the decalin series is formed by the hydrogenation of acids (XII) and (XIII) over Pt and Pd catalyst, which differ in the configuration at the 1, 9, and 10 carbon atoms (marked by the large dots). This mixture of acids was not subjected to separation into the individual isomers.

By heating 1-vinyl-Δ^1-cyclohexene with an excess of methacrylic acid, a neutral product, the lactone (XVI) was formed in addition to the acids (XII) and (XIII), which gave the crystalline hydroxyacid (XVII) by saponification with sodium methylate (aqueous and alcoholic alkali do not saponify it):



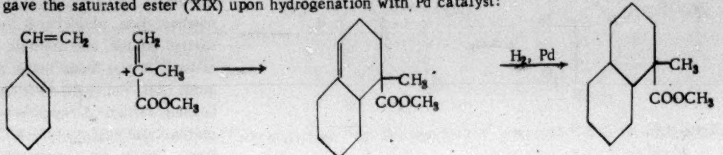
(XIV) (XVI) (XVII)

Lactone (XVI) is dehydrogenated with considerably more difficulty; in comparison to acids (XII) and (XIII) to also form α-methylnaphthalene (XIV).

The hydroxyacid (XVII) was found to be very unstable; upon attempts to esterify it, on recrystallization from hot alcohol, even when standing in the air and in the desiccator over calcium chloride, it is transformed into the starting lactone. Similar cases of lactonization of unsaturated cyclic acids have been reported in the literature [16,17,18,19]. The structures of the corresponding lactones were not stated by these authors.

By the direct lactonization of acid (XII) in the presence of methacrylic acid, lactone (XVI) could not be obtained in high yield. By heating acid (XII) with 50% sulfuric acid, the yield of lactone (XVI) is 54%. Similar examples of easy cyclization of β,γ-unsaturated cyclic acids into the corresponding lactone were recently shown in the authors' laboratory for other subjects.

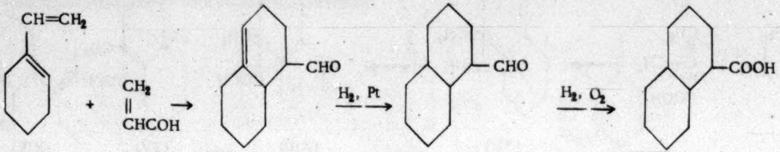
The ester (XVIII) is formed by the condensation of 1-vinyl-Δ^1-cyclohexene with methyl methacrylate, which gave the saturated ester (XIX) upon hydrogenation with Pd catalyst:



(XVIII) (XIX)

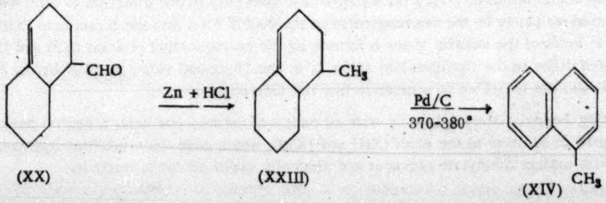
By the saponification of ester (XVIII) with alcoholic alkali a mixture of acids (XII) and (XIII) was obtained, while upon the dehydrogenation of ester (XVIII) with palladium on charcoal at 360°, α-methylnaphthalene (XIV) is obtained.

The condensation of 1-vinyl-Δ^1-cyclohexene with acrolein also occurs in the same fashion. The unsaturated aldehyde (XX) is formed, which gives the saturated aldehyde (XXI) upon hydrogenation in alcoholic solution over a Pt catalyst, while the crystalline α-decalin carboxylic acid (XXII) with m.p. 142-144°, was isolated on the oxidation of the latter with hydrogen peroxide:



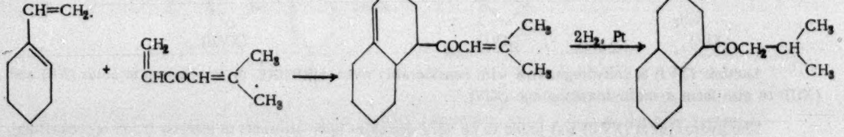
(XX) (XXI) (XXII)

The structure of aldehyde (XX) was established by its reduction into 1-methyl-Δ^4-octalin (XXIII) according to Clemmenson which gave α-methylnaphthalene (XIV) upon dehydrogenation with palladium on carbon at 370-380°:



(XX) (XXIII) (XIV)

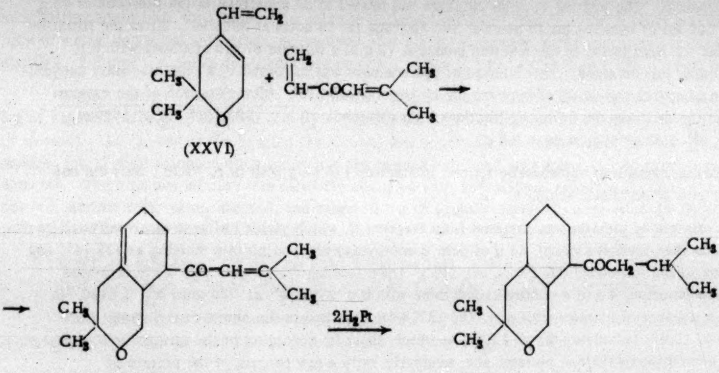
Upon the dehydrogenation of aldehyde (XX) under the same conditions, naphthalene and products of more intense decomposition are formed. The condensation of 1-vinyl-Δ^1-cyclohexene with β,β-dimethyldivinyl ketone was also effected and isobutenyl-α-Δ^4-octalyl ketone (XXIV) was formed, which on hydrogenation formed isobutyl-α-decalyl ketone (XXV):



(XXIV) (XXV)

Ketones (XXIV) and (XXV) could not be reduced by the Clemmenson method, and were dehydrogenated with difficulty with selenium and palladium on carbon. Upon the dehydrogenation of these ketones in order to obtain the known α-naphthylisobutyl ketone, a fraction was obtained which was close in composition to the corresponding ketones of the tetralin series.

2,2-Dimethyl-4-dimethyl-4-vinyl-3,6-dihydropyran (XXVI) [20] obtained in the authors' laboratory also takes part in a dienic condensation with β,β-dimethyldivinyl ketone, forming the heterocyclic ketone (XXVII) which formed the saturated ketone (XXVIII) by hydrogenation with a Pt catalyst:

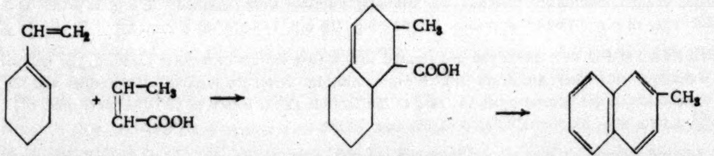


(XXVI)

(XXVII)

(XXVIII)

The dienic condensation of 1-vinyl-Δ^1-cyclohexene with crotonic acid leads to the formation of a mixture of α-acids of the hydronaphthalene series (XXIX):



(XXIX)

upon the dehydrogenation of which, with Pd on carbon (5% Pd), β-methylnaphthalene was obtained which was characterized in the form of its picrate.

EXPERIMENTAL

1-Vinyl-Δ^1-cyclohexene (b.p. 143-145°; n_D^{20} 1.4915) was obtained by the dehydration of 1-vinylcyclohexanol-1, obtained by the condensation of acetylene with cyclohexanone and the partial hydrogenation of the 1-ethynylcyclohexanol-1 in the presence of a Pd catalyst [13], with potassium bisulfate.

Condensation of 1-vinyl-Δ^1-cyclohexene with methacrylic acid. 6 g of 1-vinyl-Δ^1-cyclohexene, 5 g methacrylic acid (b.p. 74° at 20 mm; n_D^{20} 1.4300), and 0.1g pyrogallol were heated for 8 hours at 135-140°. Upon the distillation of the reaction products in vacuum, 3.5 g of the starting substances and 5 g of a mixture of acids (XII) and (XIII) with b.p. 150-152° at 4 mm, n_D^{20} 1.5100, from which 2 g of 1-methyl-Δ^4-octalin-1-carboxylic acid with m.p. 110-112° was obtained after two recrystallizations from petroleum ether.

3.954 mg substance: 10.833 mg CO_2; 3.380 mg H_2O. 5.224 mg substance: 14.269 mg CO_2; 4.430 mg H_2O. Found %: C 74.55; H 9.56, 9.61. $C_{12}H_{18}O_2$. Calculated %: C 74.22; H 9.27. 0.1423 mg substance: 7.5 ml 0.1 N KOH. Found: M 190. $C_{12}H_{18}O_2$. Calculated : M 194.

Dehydrogenation of acid (XII) with selenium and palladium on charcoal did not give satisfactory results. Satisfactory results were obtained upon dehydrogenation with a Ni catalyst.

6.5 g of acid (XII) with m.p. 110-112°, 100 ml of benzene, and 12 g of Raney Ni were heated in an autoclave for 16 hours at 370-380°. After the removal of the solvent, the residue was distilled at normal pressures and the following fractions were isolated: I) b.p. 226-230°, n_D^{22} 1.5400 - 0.8 g; II) b.p. 230-238°, n_D^{22} 1.5800-0.8 g, III) b.p. 238-241°, n_D^{22} 1.6030-3 g.

5.8 g of α-methylnaphthalene (XIV) picrate with m.p. 138-139° which did not give a depression with the known substance [21] was obtained from fraction III.

Dehydrogenation of the mixture of acids (XII) and (XIII). 30 g of 1-vinyl-Δ^1-cyclohexene, 25 g of methacrylic acid, and 1 g of pyrogallol were heated in a metallic ampoule for 12 hours at 138-140°. 33 g of a mixture of acids (XII) and (XIII) with b.p. 154-164° at 4 mm; n_D^{18} 1.5080 was obtained on the distillation of the reaction products. The mixture of acids obtained was heated in an autoclave in the presence of 40 g of Raney Ni and 100 ml of benzene for 12 hours at 300-320° and for 16 hours at 380-390°. After the filtration of the catalyst and the distillation of the reaction products, 19 g of a mixture of hydrocarbons with b.p. 210-235°, n_D^{20} 1.5980, was obtained. This mixture of hydrocarbons was subjected to a supplementary dehydrogenation with 7 g of nickel and 70 ml of benzene for 17 hours at 380-390°. After filtration of the catalyst and distillation of the product, the following fractions were obtained: I) b.p. 225-230°, n_D^{18} 1.5680—4g; II) b.p. 237-244°, n_D^{18} 1.6120—12g; residue 0.5 g.

Upon standing, crystals of naphthalene formed in Fraction I (0.05 g with m.p. 75-78°; they did not give a depression with an authentic sample).

27 g of a mixture of picrates was obtained from Fraction II, which yielded after several recrystallizations from ethyl and then methyl alcohol, 14 g of pure α-methylnaphthalene picrate melting at 138-141° and giving a depression with a known sample (m.p. 141-142°). Upon heating this picrate with a concentrated potassium carbonate solution, 4 g of α-methylnaphthylene with b.p. 239-242°, at 730 mm; n_D^{22} 1.6120. In addition, 11 g of a mixture of picrates with m.p. 130-137° were obtained in the above experiment, (Found %: N 11.76, 11.49; calculated %: N 11.32) in which, there is, according to the fusion curve, not less than 90% of α-methylnaphthalene picrate, and, evidently, only a few percent of the picrate of naphthalene itself.

Lactone (XVI). 64 g of methacrylic acid, 34 g of 1-vinyl-Δ^1-cyclohexene, and 0.5 g of pyrogallol were heated in a metallic ampoule at 138-140° for 8 hours. Upon distillation, 40 g of a mixture of starting materials, and 41 g of condensation products with b.p. 138-158° at 3 mm (residue 12 g) were obtained. Upon redistillation of the condensation products, the following fractions were obtained: I) b.p. 129-138° at 3 mm; n_D^{22} 1.4920—20g; II) b.p. 145-149° at 3 mm; 1.5080—5 g; III) b.p. 149-151° at 3 mm; n_D^{12} 1.5110—14 g.

Fractions I and II were combined and treated with a 10% sodium carbonate solution, the neutral products extracted with ether, and dried with calcium chloride. After the removal of the ether and the vacuum distillation of the neutral products, 14 g of the lactone (XVI) with b.p. 137-138° at 5 mm; n_D^{20} 1.4930; d_4^{20} 1.085; MR_D 51.96; calculated 52.66, was isolated.

7.528 mg substance: 20.50 mg CO_2; 6.353 mg H_2O. 5.270 mg substance: 14.43 mg CO_2; 4.425 mg H_2O. Found %: C 74.22, 74.72; H 9.44, 9.39. $C_{12}H_{18}O_2$. Calculated %: C 74.22; H 9.27.

The lactone does not decolorize bromine and permanganate solutions and is a neutral substance.

10 g of a mixture of acids (XII) and (XIII) with b.p. 137-142° at 2 mm, n_D^{21} 1.5100, was obtained from the acidic condensation products.

Hydrogenation of acids (XII) and (XIII). a) 4.7 g of the mixture of acids (XII) and (XIII) with n_D^{21} 1.5100 obtained in the previous experiment, was hydrogenated in 20 ml of ethyl alcohol over a Pt catalyst. After 2.5 hours, 570 ml of hydrogen (1 mole) had been added. After two distillations, 2.5 g of the saturated acid (XV) with b.p. 144-146° at 4 mm, n_D^{25} 1.5010, was isolated.

7.89 mg substance: 21.34 mg CO_2; 6.99 mg H_2O. 8.35 mg substance: 22.60 mg CO_2; 7.31 mg H_2O. Found %: C 73.85, 73.86; H 9.92, 9.74. $C_{12}H_{20}O_2$. Calculated %: C 73.46; H 10.20.

b) 5 g of a mixture of acids (XII) and (XIII) with b.p. 152-161° at 4 mm; n_D^{20} 1.5100, was hydrogenated in 50 ml of alcohol over a Pt catalyst. After 1 hour, 350 ml of hydrogen had been added; then the hydrogenation was greatly slowed down. Upon the addition of a Pd catalyst (on calcium carbonate), the rate of the hydrogenation increased, and 180 ml more of hydrogen had added in 40 minutes; a total of 530 ml of hydrogen (1 mole) had added. 4.8 g of the saturated acid (XV) with b.p. 149-154° at 4 mm, n_D^{25} 1.5035, was obtained.

c) 0.4 g of the crystalline acid (m.p. 99-103°) was hydrogenated in 10 ml of alcohol over a Pt catalyst. 40 ml (1 mole) of hydrogen had added in 4 hours. After recrystallization, saturated acid (XV) with b.p. 124-127° (from the mother liquor, m.p. 114-117°) was obtained.

Cyclization of acid (XII). 5 g of acid (XII) with m.p. 110-112° was heated in 5 ml of 50% sulfuric acid on a boiling water bath for 1 hour. The mixture darkened strongly. The reaction product was diluted with two parts of water, extracted with ether, neutralized with sodium carbonate, dried with calcium chloride, and vacuum distilled. 2.7 g of the above described lactone (XVI) with b.p. 140-143° at 9 mm, n_D^{22} 1.4940, was isolated.

Saponification of lactone (XVI). Alcoholic alkali solution did not saponify the lactone even on heating. 2 g of the lactone (b.p. 137-138° at 5 mm) was boiled for 4 hours with sodium ethylate (0.5 g of sodium, 50 ml of alcohol). At the end of the heating the alcohol was removed in vacuum, 20 ml of water was added to the residue, the alcohol removed once more, and the residue extracted with ether, but no neutral products were detected. The aqueous solution was carefully acidified with 50% sulfuric acid; the crystals which separated were filtered, washed with water, alcohol, and ether. 2.5 g of slightly yellowish crystals of the hydroxy acid (XVII) with m.p. 97-101° was isolated.

6.842 mg substance: 16.413 mg CO_2; 5.793 mg H_2O. 6.648 mg substance: 16.000 mg CO_2; 5.635 mg H_2O. Found %: C 65.47, 65.68; H 9.47, 9.48. $C_{12}H_{20}O_3 \cdot \frac{1}{2} H_2O$. Calculated %: C 65.16; H 9.50.

Upon standing and attempts to recrystallize, the crystals of hydroxy acid (XVII) melted and were once more transformed into lactone (XVI); (b.p. 129-130° at 2 mm; n_D^{23} 1.4920).

10.14 mg substance: 27.58 mg CO_2; 8.54 mg H_2O. Found %: C 74.23; H 9.42. $C_{12}H_{18}O_2$. Calculated %: C 74.22; H 9.27.

Dehydrogenation of lactone (XVI). 9 g of the lactone (b.p. 138-139° at 4 mm, n_D^{20} 1.4930), 18 g of Raney Ni, and 100 ml of benzene were heated for 23 hours at 380-390°. After filtration of the catalyst and the distillation of the product, the following fractions were obtained: I) b.p. 180-220°; n_D^{20} 1.5440 −1.4 g; II) b.p. 220-225°; n_D^{20} 1.5880 −2.4 g.

The fractions obtained were subjected to a supplementary dehydrogenation with 5 g of nickel in 50 ml of benzene at 370-390° for 21 hours. The following fractions were obtained upon distillation: I) b.p. 215-220°, n_D^{20} 1.5880 −1.2 g; II) b.p. 225-232°; n_D^{20} 1.5980 −1 g; residue −1 g.

Fraction II (b.p. 225-232°) was treated with a conc. alcoholic solution of picric acid, and α-methylnaphthylene picrate with m.p. 137-138° was isolated from the picrates obtained by fractional crystallization from alcohol, which did not give a depression with a known sample. In addition, 0.1 g of a picrate with m.p. 131-132° whose analysis also corresponded to methylnaphthalene picrate was isolated.

4.840 mg substance: 0.480 ml nitrogen (23°, 753 mm). 4.935 mg substance: 0.490 ml nitrogen (24°, 777 mm). Found %: N 11.33, 11.22. $C_{17}H_{13}O_7N_3$. Calculated %: N 11.32.

Condensation of 1-vinyl-Δ^1-cyclohexene with methyl methacrylate. 10 g of 1-vinyl-Δ^1-cyclohexene, 10 g of methyl methacrylate (b.p. 99-101°, n_D^{20} 1.4130), 5 g of dioxane, and 0.2 g of pyrogallol were heated in a metallic ampoule for 8 hours at 140°. Upon distillation of the reaction products, 5 g of a mixture of starting substances and 12 g of ester (XVIII) with b.p. 111-112° at 4 mm; n_D^{20} 1.4940; d_4^{20} 1.0346; MR_D 59.45; calculated, 59.02, were obtained.

9.47 mg substance: 26.80 mg CO_2; 8.35 mg H_2O. 12.27 mg substance: 33.69 mg CO_2; 10.66 mg H_2O. Found %: C 75.09, 74.93; H 9.59, 9.72. $C_{13}H_{20}O_2$. Calculated %: C 75.00; H 9.61.

Saponification of ester (XVIII). 19 g of the ester was heated with 150 ml of 10% methanol solution of potassium hydroxide for 6 hours on a water bath. At the end of the heating, the methyl alcohol was removed, the residue was diluted with water (40 ml), extracted with ether, and acidified with 25% sulfuric acid. The organic acids were extracted with ether, dried with sodium sulfate, vacuum distilled. 12 g of the above reported mixture of acids (XII) and (XIII) with b.p. 157-158° at 5 mm, n_D^{20} 1.5115, was obtained.

10.10 mg substance: 27.10 mg CO_2; 8.33 mg H_2O. 21.65 mg substance: 58.88 mg CO_2; 17.85 mg H_2O. Found %: C 73.96, 74.22; H 9.32, 9.24. $C_{12}H_{18}O_2$. Calculated %: C 74.22; H 9.27.

Upon standing this mixture of acid partially crystallized and the following fractions were separated: I) m.p. 92-105° – 2.8 g; II) m.p. 58-85° – 2.5 g; III) – liquid – 5 g.

9 g of the mixture of acids obtained by the saponification of ester (XVIII), was dissolved in 40 g of a mixture of glacial acetic acid and hydrogen chloride (10% HCl). After 15 minutes, the solution was poured into water, the mixture extracted with ether, and the ether solution dried with calcium chloride. After removal of the ester and distillation of the reaction products, the following products were obtained:

I) B.p. 115-134° at 5 mm, n_D^{18} 1.4990 – 1 g; II) b.p. 134-136° at 5 mm, n_D^{18} 1.500 – 5 g; residue – 2 g.

Fractions I and II were combined, treated with 10% sodium carbonate solution, the neutral products extracted with ether, and dried with calcium chloride. After removal of the ether and the distillation of the products, 3.4 g of lactone (XVI) with b.p. 133-135° at 5 mm, n_D^{19} 1.4950, was obtained. Only several drops of an acid with n_D^{22} 1.5100 was isolated.

Hydrogenation of ester (XVIII). 5 g of ester (b.p. 111-112° at 4 mm) was hydrogenated in 20 ml of ethyl alcohol over a Pd catalyst (the ester was not hydrogenated over a Pt catalyst). 510 ml of hydrogen (1 mole) had added in 3 hours. As a result of the distillation of the hydrogenation product in vacuum: 4.7 g of methyl-1-methyl-2-decalin carboxylate (XIX) with b.p. 100-102° at 2 mm, n_D^{20} 1.4840; d_4^{20} 1.0192.

4.008 mg substance: 10.842 mg CO_2; 3.558 mg H_2O. 4.870 mg substance: 13.194 mg CO_2; 4.460 mg H_2O. Found %: C 73.81, 73.91; H 9.93, 10.20. $C_{13}H_{22}O_2$. Calculated %: C 74.28; H 10.27.

Dehydrogenation of ester (XVIII). 2.2 g of ester (XVIII), 1 g of palladium on carbon (5% Pd) and 15 ml of benzene were heated for 10 hours at 860-370°. The solution was filtered, the catalyst was washed several times with benzene, the benzene was removed at atmospheric pressure, and the residue vacuum distilled; the following fractions were obtained: I) b.p. 110-116° at 18 mm – 0.1 g; II) b.p. 116-118° at 18 mm, n_D^{20} 1.5970 – 0.85 g.

1.3 g of α-methylnaphthalene picrate was isolated from Fraction 2 by the action of a concentrated alcoholic picric acid solution, m.p. 138-140° (from alcohol); it did not give a depression with a known sample.

Saponification of the saturated ester (XIX). 5 g of ester (XIX) was heated on a water bath with 50 ml of a 20% alcoholic solution of potassium hydroxide for 24 hours. At the end of the reaction, the alcohol was removed in vacuum, the residue was diluted with water, and extracted with ether to remove the neutral substances. The aqueous solution was acidified with 20% sulfuric acid, the organic acids were extracted with ether, and dried with sodium sulfate. Upon distillation, 2 g of a mixture of acids with b.p. 142-154° at 4 mm were isolated in the form of a colored thick liquid.

Condensation of 1-vinyl-Δ^1-cyclohexene with acrolein. 20 g of 1-vinyl-Δ^1-cyclohexene, 12 g of acrolein (b.p. 52-53°, n_D^{14} 1.4020) and 0.3 g of pyrogallol were heated in a glass ampoule for 5 hours at 110-115°. Upon the distillation of the products, 2.7 g of mixture of starting substances and 24 g of aldehyde (XX) with b.p. 100-101° at 5 mm, n_D^{20} 1.5098; d_4^{20} 1.0239; MR_D 47.92; calculated 48.14, were isolated.

11.27 mg substance: 33.11 mg CO_2; 9.97 mg H_2O. 9.23 mg substance: 27.10 mg CO_2; 8.50 mg H_2O. Found %: C 80.17, 80.12; H 9.90, 10.30. $C_{11}H_{16}O$. Calculated %: C 80.48; H 9.75.

The semi-carbazone of the aldehyde (XX) melted at 190-191° (from alcohol).

4.662 mg substance: 0.774 ml nitrogen (21°, 736 mm). 4.790 mg substance: 0.799 ml nitrogen (20°, 735 mm). Found %: N 18.67, 18.79. $C_{12}H_{19}ON_3$. Calculated %: N 19.00.

Hydrogenation of aldehyde (XX). 10 g of aldehyde (b.p. 100-101° at 5 mm) was hydrogenated in 40 ml of methyl alcohol over a Pt catalyst. 1.3 liters (1 mole) of hydrogen had added in 13 hours. After two distillations, 9.5 g of the saturated aldehyde (XXI) with b.p. 100-102° at 7 mm, n_D^{22} 1.4950, was isolated. The semicarbazone of this aldehyde melted at 182-183° (from alcohol).

3.965 mg substance: 0.641 ml nitrogen (23°, 753 mm). 3.740 mg substance: 0.607 ml nitrogen (24°, 759 mm). Found %: N 18.47, 18.63. $C_{12}H_{21}ON_3$. Calculated %: N 18.83.

Oxidation of aldehyde (XXI). 2.4 g of the aldehyde (b.p. 100-102° at 7 mm) was heated with 60 ml of hydrogen peroxide for 4 hours until the disappearance of the upper layer. An oily layer which formed on the bottom of the flask was separated, dissolved in ether, and the ether solution was dried over sodium sulfate. After the removal of the ether, the residue crystallized (2 g). After two recrystallizations from methyl alcohol, 1 g of acid (XXII) with m.p. 142-144° was obtained.

4.405 mg substance: 11.800 mg CO_2; 3.585 mg H_2O. 4.670 mg substance: 12.520 mg CO_2; 3.745 mg H_2O. 0.1558 g substance: 8.78 ml 0.1 N KOH. Found %: C 73.10, 73.16; H 9.10, 8.97; M 178. $C_{11}H_{18}O_2$. Calculated %: C 72.51; H 8.98; M 182.

Reduction of aldehyde (XX) according to Clemmenson. 4 g of the aldehyde (b.p. 100-101° at 5 mm) dissolved in 25 ml of ethyl alcohol was added to a boiling mixture of amalgamated zinc, 5 ml of water, and 15 ml of hydrochloric acid. The product was diluted with water (50 ml), neutralized with sodium carbonate, extracted with ether, and dried over calcium chloride. After two distillations, 1.5 g of hydrocarbon (XXIII) with b.p. 85-87° at 13 mm, n_D^{20} 1.4990; d_4^{20} 0.9294 was obtained.

6.210 mg substance: 19.852 mg CO_2; 6.650 mg H_2O. 4.350 mg substance: 13.905 mg CO_2; 4.640 mg H_2O. Found %: C 87.22, 87.20; H 11.99, 11.92. $C_{11}H_{18}$. Calculated %: C 88.00; H 12.00.

Dehydrogenation of hydrocarbon (XXIII). 0.8 g of the hydrocarbon (b.p. 85-87° at 13 mm), 0.8 g of palladium on carbon (5% Pd) and 20 ml of benzene were heated for 10 hours at 370-380°. At the end of the heating, the mixture was filtered from the catalyst, the benzene removed, and the residue vacuum distilled. 4.5 g of a substance with b.p. 100-103° at 10 mm was obtained from which 0.6 g of a picrate with m.p. 138-139° (from alcohol, not giving a depression with α-methylnaphthalene picrate) was obtained by the action of a conc. solution of picric acid.

Condensation of 1-vinyl-Δ^1-cyclohexene with β,β-dimethyldivinyl ketone. 15 g of 1-vinyl-Δ^1-cyclohexene, 20 g of β,β-dimethyldivinyl ketone (b.p. 45-46° at 11 mm, n_D^{15} 1.480 [22]) and 0.1 g of pyrogallol were heated in a glass ampoule for 10 hours at 125-130°. The solution thickened greatly. Upon the distillation of the products of the condensation, 7 g of a mixture of starting substances and 10 g of the unsaturated ketone (XXIV), with b.p. 139-140° at 4 mm, n_D^{20} 1.5205; d_4^{20} 1.0001; MR_D 66.39; calculated 66.14 were obtained.

6.035 mg substance: 18.220 mg CO_2; 5.442 mg H_2O. 5.965 mg substance: 18.000 mg CO_2; 5.385 mg H_2O. Found %: C 82.39, 82.35; H 10.09, 10.10. $C_{15}H_{22}O$. Calculated %: C 82.57; H 10.09.

Crystalline derivatives of the ketone (XXIV) could not be obtained.

Hydrogenation of ketone (XXIV). 2 g of the ketone (b.p. 139-140° at 4 mm) was hydrogenated in 30 ml of ethyl alcohol over a Pt catalyst. 440 ml (2 moles) H had added in 50 minutes. As a result of the distillation, 1.5 g of the saturated ketone (XXV) with b.p. 127-128° at 4 mm, n_D^{20} 1.4810; d_4^{20} 0.9465; MR_D 66.62; calculated 67.07, was obtained.

11.42 mg substance: 33.63 mg CO_2; 11.87 mg H_2O. Found %: C 80.36; H 11.64. $C_{15}H_{26}O$. Calculated %: C 81.08; H 11.72.

Upon the preparation of the semicarbazone, an oil which could not be crystallized came out.

The ketone did not reduce according to Clemmenson. Upon the dehydrogenation of ketones (XXIV) and (XXV) with the aim of preparing the known α-naphthyl isobutyl ketone with palladium on carbon (5% Pd) for 6 hours at 350°, a mixture was obtained which was close to the ketones of the tetralin series by its composition.

Dehydrogenation of ketones (XXIV) and (XXV) with selenium also did not lead to satisfactory results.

Condensation of 2,2-dimethyl-4-vinyl-3,6-dihydropyrane with β,β-dimethyldivinyl ketone. 5 g of 2,2-dimethyl-4-vinyl-3,6-dihydropyrane (XXVI) (b.p. 84° at 40 mm, n_D^{20} 1.4830), 6 g of dimethyldivinyl ketone (b.p. 44 at 10mm, n_D^{15} 1.4815), and 0.1 g of pyrogallol were heated for 6 hours in a glass ampoule to 120-125°. After the distillation of the reaction products, 5.8 g of ketone (XXVII) with b.p. 153)155° at 4 mm; n_D^{20} 1.5175; d_4^{20} 1.0279; MR_D 73.02; calculated 72.40, was isolated.

7.600 mg substance: 21.472 mg CO_2; 6.577 mg H_2O. 5.248 mg substance: 14.847 mg CO_2. 4.550 mg H_2O. Found %: C 77.10, 77.21; H 9.68, 9.70. $C_{16}H_{24}O_2$. Calculated %: C 77.41; H 9.68.

Hydrogenation of ketone (XXVII). 2 g of the ketone (b.p. 153-155° at 4 mm) was hydrogenated over a Pt catalyst in 20 ml of ethyl alcohol. 320 ml of hydrogen (2 moles) had added in 1.5 hours. 1.5 g of the saturated ketone (XXVIII) with b.p. 127-129° at 7 mm, n_D^{20} 1.4865; d_4^{20} 0.9865; MR_D 73.49; calculated 73.33 was isolated.

5.380 mg substance: 15.045 mg CO_2; 5.140 mg H_2O. 5.470 mg substance: 15.245 mg CO_2; 5.205 mg H_2O. Found %: C 76.31, 76.06; H 10.69, 10.64. $C_{16}H_{28}O_2$. Calculated %: C 76.19; H 11.11.

Upon the preparation of the semicarbazone and 2,4-dinitrophenyl hydrazone, an uncrystallizable oil was obtained.

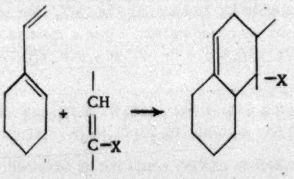
Condensation of 1-vinyl-Δ^1-cyclohexene with crotonic acid. 7.8 g of 1-vinyl-Δ^1-cyclohexene, 6 g of crotonic acid (m.p. 71-72°), 3 ml of dioxane were heated for 8 hours to 145°. After the removal of the dioxane and the unreacted starting materials, and vacuum distillation of the product, 3 g of a mixture of acids (XXIX) with b.p. 138-142° at 4 mm, n_D^{30} 1.4990 was obtained.

8.81 mg substance: 23.76 mg CO_2; 7.37 mg H_2O. 11.96 mg substance: 32.23 mg CO_2; 9.99 mg H_2O. 0.1645 g substance: 8.6 ml 0.1 N NaOH. Found %: C 73.60, 73.54; H 9.35; 9.34; M 193. $C_{12}H_{18}O_2$. Calculated %: C 74.22; H 9.27, M 194.

Dehydrogenation of acids (XXIX). 2 g of the acids with b.p. 138-142° at 4 mm, 1 g Pd on carbon (5% Pd) and 10 ml of benzene were heated for 15 hours to 360-370°. After the removal of catalyst and the distillation of the benzene, 0.8 g of picric acid (concentrated solution) was added to the residue, and 0.4 g of picrate with m.p. 112-113° (from alcohol) not giving a depression with α-methylnaphthalene picrate, was obtained.

SUMMARY

1-Vinyl-Δ^1-cyclohexene, upon dienic condensation with methyl methacrylate, methacrylic acid, acrolein, and other asymm. dienophiles, forms α-substituted derivatives of octahydronaphthalene according to the following scheme:



There were no β-substituted octahydronaphthalenes detected during these condensations.

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*** See Consultants Bureau English translation, page 273.

**** See Consultants Bureau English translation.

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REACTION OF DIPHENYL MERCURY WITH CARBON TETRACHLORIDE

G. A. Razuvaev and Yu. A. Oldekop

The great inertness of diphenyl and o-tolyl mercury toward various polyhalides was mentioned in the papers of Whitman and Thurman [1]. Upon prolonged heating of diphenyl mercury with carbon tetrachloride (up to 350 hours), there was no reaction between the components. Analogously, no reaction was found with other halides (ethylidene chloride, benzylidene chloride, benzotrichloride, dichloroethyl acetate, cyclohexyl bromide, and others). Koton, Zorina, and Osberg [2] also did not observe a reaction between diphenyl mercury and chloroform and bromoform, upon heating in sealed tubes to 130°. A reaction occurred only between diphenyl mercury and iodoform. At the same time, the authors [3] showed that radiation with ultraviolet light, even at ordinary temperatures, caused a reaction between R_2Hg and halo derivatives to occur. For carbon tetrachloride, the reaction occurred according to the following summary equation:

$$R_2Hg + 2CCl_4 \longrightarrow RHgCl + RCl + C_2Cl_6$$

The reaction also occurred by the action of benzoyl peroxide on a solution of diphenyl mercury in carbon tetrachloride [4]. Phenyl mercuric chloride, chlorobenzene, hexachloroethane, mercuric salts of benzoic and ω-trichlorotoluic acid were found in the reaction products.

Recently, Borisov [5] was able to show that the separation of phenyl mercuric chloride and the formation of benzotrichloride occurred upon the action of acetyl peroxide on a solution of diphenyl mercury in carbon tetrachloride. The reaction between diphenyl mercury and chloroform occurs with the separation of phenyl mercuric chloride, benzene, and only traces of benzotrichloride. The fact that hexachloroethane, but not benzotrichloride is formed by the action of light, seems strange. For many reactions which occur between carbon tetrachloride and other compounds, the action of ultraviolet light and peroxides leads to identical products [6].

For this reason it appeared interesting to conduct a thermal reaction between diphenyl mercury and carbon tetrachloride. It appeared that the inertness of these compounds was explained by the extremely low temperature at which the above investigators worked and in fact, upon heating above 200°, a reaction occurred between carbon tetrachloride and diphenyl mercury as expressed by the equation:

$$(C_6H_5)_2Hg + CCl_4 \longrightarrow C_6H_5HgCl + C_6H_5CCl_3$$

Therefore, the thermal reaction was found to be identical with the reaction produced by peroxides.

From the results given in the Table, it is apparent that the end products of the decomposition of diphenyl mercury increase in quantity with increase in reaction temperature and time. In fact, at 270°, phenyl mercuric chloride could not be seen; only mercuric chloride and a large amount of calomel were found.

It is interesting to mention that differences in reactions of carbon tetrachloride by the action of heat and by the action of ultraviolet illumination were also noted in other cases. Thus, by the illumination of a mixture of methanol and carbon tetrachloride, the formation of hexachloroethane according to the equation:

$$CH_3OH + 2CCl_4 \longrightarrow CH_2O + 2HCl + C_2Cl_6$$

occurred, whereas chloroform is formed by heating [7] :

$$CH_3OH + CCl_4 \longrightarrow CH_2O + HCl + CHCl_3.$$

Further study is required to explain such differences in the reactions of carbon tetrachloride.

EXPERIMENTAL*

The experiments were conducted in sealed glass tubes placed inside iron tubes while they were heated in an electric furnace. The thermometer was found between the iron tube and the electric furnace. Therefore, the temperature determination was rather rough; for this reason separate experiments were conducted in small sealed glass ampoules placed into the oil of a thermostat in order to determine the start of reaction.

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* The experimental work was conducted with the aid of G. F. Cheloginsov.

The orienting experiments showed that the reaction between diphenyl mercury and carbon tetrachloride started at 210°.

5.0 g of diphenyl mercury and 25 ml of carbon tetrachloride were charged into the sealed tube, and the reaction mixture heated for 23 to 60 hours (See Table).

Temperature	Heating time (hours)	Reaction Products							
		Phenyl mercuric chloride		Calomel		Mercuric chloride		Benzoic acid (g)	p-nitrochlorobenzene (g)
		(g)	(%)	(g)	(%)	(g)	(%)		
230°	23	3.45	78.4	0.1	3.0	—	—	0.51	0.98
230	42	2.50	56.8	1.03	31.0	—	—	0.65	0.50
250	35	0.6	13.6	0.3	9.1	2.55	66.6	0.1	0.40
260	27	0.1	2.3	0.67	20.2	2.8	73.1	0.35	0.50
270	20	—	—	1.7	51.2	1.3	34.0	0.4	0.37

At the end of the reaction, the precipitate was filtered. Phenyl mercuric chloride was separated from it by solution in acetone. After recrystallization from the same solvent, it had an m. p. 257° without depressing the melting point of an authentically pure phenyl mercuric chloride. Mercuric and mercurous chloride remained in the residue. Mercuric chloride was removed by solution in ethyl alcohol. It was identified by reaction for the mercuric ion. The part insoluble in alcohol was calomel. The filtrate was made alkaline with potassium hydroxide and steam distilled. The distillate was nitrated directly after the removal of water. The nitro product isolated was 2,4-dinitrochlorobenzene with m. p. 51-52°. In isolated cases, p-nitrochlorobenzene with m. p. 82° was obtained. Both nitro products did not give a depression in melting point with authentic pure preparations of 2,4-dinitrochlorobenzene and p-nitrochlorobenzene, respectively.

The residue after steam distillation was filtered, and the benzoic acid was precipitated with mineral acid. Benzoic acid, after ether extraction and isolation, was recrystallized from alcohol, and had an m. p. 119-120°. A mixed sample with authentic pure benzoic acid give an m. p. 120°.

SUMMARY

On heating diphenyl mercury and carbon tetrachloride above 200° in sealed tubes, a reaction occurred forming phenyl mercuric chloride and benzotrichloride.

On increasing the temperature to 270°, or increasing the reaction time, a complete de-arylization of diphenyl mercury occurred to form calomel and mercuric chloride.

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REACTION OF ACYL PEROXIDES WITH METALLIC MERCURY

G. A. Razuvaev, Yu. A. Oldekop, and L. N. Grobov

Recently, the reactions of free radicals in solutions have been studied very intensely. These types of reactions are of great theoretical and practical interest, since they make it possible to explain mechanisms of industrially important chemical processes such as, for example, polymerization of unsaturated compounds, auto-oxidation, addition to multiple bonds, etc. A successful method for proof of the formation of free radicals in chemical reactions is their fixation on elements. This method is equally applicable to the investigation of processes occurring in the gaseous and liquid phases.

The simplest radicals, methyl and ethyl, were shown in the gaseous phase with this method [1]. The phenyl radical was shown during the decomposition of phenyl diazonium chloride in the liquid state by its fixation on elements [2], where phenyl derivatives of the elements were formed in the case of mercury, arsenic, antimony, and tellurium. Analogously, phenylmercury was formed by the decomposition of benzene diazoacetate in non-polar solvents, for example carbon tetrachloride, in the presence of mercury [3]. Upon boiling diphenyl iodonium iodide in propyl alcohol in the presence of mercury, antimony, or tellurium, a transfer of the phenyl radicals to the elements occurs with the formation of metallo-organic derivatives of the latter [4]. The formation of phenyl radicals was shown upon the decomposition of benzoyl peroxide in carbon tetrachloride solution in the presence of metallic mercury [5]. The phenyl radicals were fixed in the form of phenyl mercury chloride. Phenyl radicals forming during the decomposition of benzene azotriphenylmethane in carbon tetrachloride solution were fixed in the form of phenyl mercury chloride on metallic mercury [6].

As far as is known, the fixation of alkyl radicals in the liquid phase has not been reported in the literature at all. One of these types of reactions, which gives methyl radicals, is the thermal decomposition of acetyl peroxide. The most accepted decomposition reaction of acetyl peroxide is the following:

$$(CH_3CO_2)_2 \longrightarrow CH_3\cdot + CO_2 + CH_3COO.$$

The thermal decomposition reaction of acetyl peroxide was effected in carbon tetrachloride and benzene at the boiling point of the solvents in the presence of metallic mercury. Experiments conducted on the thermal decomposition of the peroxide in carbon tetrachloride in the presence of mercury (see Table) at the boiling point showed that Hg⁺acetate, as well as Hg^+ and Hg^{++} chlorides are formed during the reaction, i. e., the same type of chlorination of mercury by carbon tetrachloride occurs as was found by the action of light on these components or with benzoyl peroxide [7]. As is known, the thermal decomposition of acetyl peroxide at about 77-80° (boiling

	Experiment No.			
	1	2	3	4
Starting substances:				
Hg (in g)	100	100	100	200
$(CH_3CO_2)_2$ (in g)	4.2	11.7	12.8	24.6
CCl_4 (in ml)	200	215	250	600
Experimental conditions:				
Addition time of the peroxide (in hours)	3	10	12	20
Time of subsequent heating (in hours)	–	2	11	14
Total time (hours)	4	12	23	34
Products isolated:				
CH_3COOHg (in g and in %)	2.7(32.7)	10.2 (45.1)	25.2(87.2)	51.6(95.6)
Hg_2Cl_2 (in g)	Determined qualitatively	1.43	6.44	17.62
$HgCl_2$ (in g)	1.14	3.81	-	-
C_2Cl_6 (in g)	0.20	2.70	4.17	5.50
Unreacted peroxide (in%)	10.5	11.9	0	0

points of carbon tetrachloride and benzene) proceeds very slowly; for this reason a very long heating was required.

In all experiments , the characteristic odor of the alkyl derivatives of mercury was noticed during the processing of the reaction mass. The amount of these derivatives was so small that they could only be detected in the last experiment by an indirect method.

Therefore, it must be assumed that acetyl peroxide reacts with mercury only by means of the acetoxy radical to form the acetate of monovalent mercury, while the reactive methyl radical formed during the experiment reacts with carbon tetrachloride:

$$\begin{gathered}(CH_3CO_2)_2 \longrightarrow CH_3\cdot + CO_2 + CH_3COO\cdot \\ CH_3COO\cdot + Hg \longrightarrow CH_3COOHg \\ CH_3\cdot + CCl_4 \longrightarrow CH_3Cl + CCl_3\cdot \\ CCl_3\cdot + CCl_4 \longrightarrow CCl_3{-}CCl_3 + Cl\cdot \\ Cl\cdot + Hg \longrightarrow HgCl.\end{gathered}$$

Studying the results of these experiments in carbon tetrachloride solution, it appeared interesting to conduct a similar series of experiments in benzene solution. As is known, [8], benzene is very unreactive to attacks by alkyl radicals. And, actually, methyl mercury acetate was obtained in a preparative yield (64.7%). Benzene was found to be an inert solvent in this case.

The reaction can be represented as proceeding according to the following equation:

$$Hg + (CH_3CO_2)_2 \longrightarrow CH_3HgOCOCH_3 + CO_2.$$

Methyl mercury acetate was converted to methyl mercury iodide with potassium iodide for convenience of isolation.

As it was shown previously [5], phenyl mercury chloride was obtained only in small yields by the thermal decomposition of benzoyl peroxide in carbon tetrachloride solution in the presence of mercury. For this reason, it appeared interesting to conduct such a reaction in benzene solution. Upon a prolonged shaking of a benzoyl chloride solution with metallic mercury, only the reaction of the formation of the benzoate of monovalent mercury was observed. Upon the heating of the benzoyl peroxide benzene solution to boiling with energetic stirring with metallic mercury the formation of phenyl mercurobenzoate occurred:

$$Hg + (C_6H_5CO_2)_2 \longrightarrow C_6H_5HgOCOC_6H_5 + CO_2.$$

The yield of the latter was 31.5%. It must be mentioned that the known reaction with benzoyl peroxide and benzene forming diphenyl occurs simultaneously with that of the transfer of the phenyl radical to the mercury; the former reaction certainly decreases the yield of the metallo-mercury compound Nevertheless, the yield of the latter is high enough to warrant a preparative interest. As for the methyl mercury derivatives, obtained by means of acetyl peroxide, this method is of considerable interest. Therefore, by using acetyl peroxide, it seems that a new method for the synthesis of metallo-organic derivatives of mercury can be developed.

EXPERIMENTAL

Reaction between acetyl peroxide and mercury in carbon tetrachloride solution. Acetyl peroxide was prepared from acetic anhydride and potassium peroxide without separation in the free form.

10 g of potassium peroxide and 100 ml of carbon tetrachloride were placed in a wide necked open flask or beaker. The reaction mixture was cooled with ice and salt to −10°. Acetic anhydride was then added dropwise with stirring and prolongation of the cooling. After addition of all of the acetic anhydride, the stirring was continued for about 1 hour more. Then ice was added, in small pieces at first, then in larger ones, until the complete decomposition of potassium peroxide. The carbon tetrachloride layer was separated from the water, washed with water, and dried with anhydrous sodium sulfate. The amount of peroxide obtained was determined by iodometric titration.

Metallic mercury, with a small layer of pure carbon tetrachloride on top of it, was placed into a three necked flask equipped with a mechanical stirrer with a mercury seal, dropping funnel, and reflux condenser. The carbon tetrachloride was heated to boiling and the carbon tetrachloride solution of acetyl peroxide was added in small portions into the flask from the dropping funnel, the end of which dipped into the carbon tetrachloride, with simultaneous stirring. The addition of acetyl peroxide took several hours, and the heating was then continued for several hours more after the addition of all of the peroxide (see the Table). Within 10-15 minutes from the start of the addition of the peroxide into the flask, a whitening of the liquid occurred, which gradually increased. The metallic mercury was separated mechanically and the rest of contents of the flask were steam distilled. Calomel was obtained in the residue. The contents of the flask were filtered while hot. The residue obtained on the filter was washed many times with hot water. The calomel in the washed residue was quantitatively determined by fusion with alkali and determination of the chloride ion.

After cooling, white crystals of the acetate of monovalent mercury separated from the filtrate (corresponding tests for Hg^+ were effected with HCl, KOH, NH_3, Na_2CO_3, and KI, as well as those for the acetate ion). The distillate from the steam distillation was separated into aqueous and carbon tetrachloride layers. Mercuric chloride was determined in the aqueous layer. Hexachlorethane, m. p. 186° (closed capillary) was isolated from the carbon tetrachloride layer after distillation. A mixed melting point with pure hexachlorethane gave no depression.

Reaction between acetyl peroxide and mercury in benzene solution. The synthesis of acetyl peroxide in benzene was effected under condition analogous to those reported for carbon tetrachloride. A rapidly moving stirrer prevented the freezing of the benzene. The benzene solution of the corresponding processing was dried with anhydrous $CaCl_2$. The yield of the peroxide was 48% of the theoretical. The experiment was conducted under conditions analogous to those when carbon tetrachloride served as the medium. A benzene solution of 9.9 g of acetyl peroxide in 200 ml of benzene was added from a dropping funnel to 100 g of mercury covered with benzene. The addition of the peroxide was continued slowly and was ended after 8 hours while heating, the reaction mass on a water bath. The benzene solution was then heated for 12 hours more.

At the end of the reaction, the benzene layer was separated from the mercury and washed many times with water. Upon the addition of a saturated solution of potassium iodide to this water, a white precipitate, methyl mercury iodide formed in a 18.6 g quantity or 64.7% of the theoretical calculated on the peroxide taken. M. P. 144-155° No depression was found with methyl mercury iodide prepared from a different source. Iodine was added to the washed benzene solution. After the distillation of the benzene, 1.23 g of mercury iodide and 1.78 g of a tarry residue, which was not further investigated, were obtained. Only traces of mercurous acetate were detected.

Reaction between benzoyl peroxide and mercury in benzene solution. The reaction was effected in a flask equipped with a mercury sealled stirrer and condenser. 200 g of mercury and 150 ml of benzene were used for the reaction. Benzoyl peroxide was added for 6 hours during the heating of the reaction mass on the water bath. The heating was continued for 14 hours more after the addition of the benzoyl peroxide. A total of 20 g of benzoyl peroxide was added (or 17.5 g calculated on a 100% basis). Its activity was determined by iodometric titration. At the end of the reaction, the benzene layer was poured from the mercury and distilled from a Wurtz flask on a water bath. A saturated solution of calcium chloride was added to the residue which crystallized, and all was steam distilled.

The residue remaining in the flask after the steam distillation was filtered and recrystallized from acetone. It was found to be phenyl mercury chloride, m. p. 254° ; no depression in melting point was found with authentic phenyl mercury chloride. The weight of the residue was 7.12 g, or 31.5% calculated on the benzoyl peroxide used. 0.53 g of diphenyl with m. p. 68-69° was collected during the steam distillation. In addition, a small amount of organic acids were isolated during the reaction, which were not investigated further.

Reaction between benzoyl peroxide and mercury in benzene solution at room temperature. 100 g of mercury and 150 g of benzene were charged into a 1-liter bottle with a ground glass stopper. 10 g of benzoyl peroxide was introduced over 20 hours (containing 8.7 g calculated on 100% basis). The shaking was continued for 100 hours more, and the mercury was then mechanically separated. An excess of a saturated calcium chloride solution was added to the contents, and the reaction was steam distilled. After the distillation of the solvent, 3.7 g or 22% of the theoretical of calomel based on benzoyl peroxide used, was obtained in the residue. Benzoic acid was also isolated -4.0 g was collected.

SUMMARY

1. The possibility for identifying alkyl radicals (for example methyl radicals) in the liquid phase by fixation on mercury was first shown.

2. Methyl mercury acetate was obtained in a yield of 64.7% by the thermal decomposition of acetyl peroxide in benzene in the presence of metallic mercury.

3. A new method for the synthesis of phenyl derivatives of mercury of the type C_6H_5HgX formed by the thermal decomposition of benzoyl peroxide in benzene in the presence of metallic mercury is given. Phenyl mercury benzoate was obtained in a 31.5% yield.

4. The thermal decomposition of acyl peroxide in the presence of metallic mercury can be a synthetic method for the preparation of alkyl and aryl metallo-organic derivatives of mercury.

5. Upon the thermal decomposition of acetyl peroxide in carbon tetrachloride in the presence of metallic mercury, the formation of mercurous acetate occurs, along with the chlorination of mercury with carbon tetrachloride initiated by the peroxide.

6. Benzoyl peroxide in benzene solution at room temperature gives mercurous benzoate.

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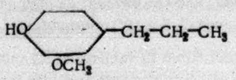
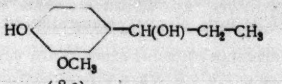
* See Consultants Bureau English translation, page. 1219.

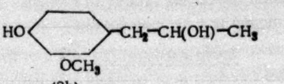
CLEAVAGE OF LIGNIN WITH METALLIC SODIUM IN LIQUID AMMONIA. V.

A. F. Semechkina and N. N. Shorygina

In the previous communications [1,2,3,4,5] it was shown that fir lignin was decomposed by the action of a solution of metallic sodium in liquid ammonia into lower molecular substances, among which were isolated dihydroeugenol (1) and 1-(4-hydroxy-3-methoxyphenyl)propanol (2a) or (2b):


(1)


(2 a)

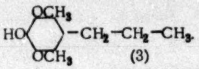

(2b)

It was proposed that formula (2b) was more correct for the propanol isolated than formula (2a).

In the present investigation lignin isolated from aspen wood by the copper ammonium method, was subjected to decomposition with metallic sodium in liquid ammonia. The experimental conditions and method of processing of the reaction mixture were analogous to those reported previously for experiments with fir lignin.

It was found that aspen lignin was more extensively cleaved under those conditions than fir lignin. Thus, by one treatment of aspen lignin with sodium in liquid ammonia, 17.66% (I + II) of monomeric substances soluble in ether and 10% (IV) of lower molecular substances soluble in water were obtained; 45.2% of uncleaved lignin (III) was obtained. Previously, 9.14% of (I) + (II) and 79.5% of (III) were obtained from fir lignin.

Upon a second treatment of aspen lignin with sodium in liquid ammonia, 6.5% of (Ia) + (IIa) and 65% of (IIIa) of the substance used in the reaction were obtained. Two fractions were obtained by the vacuum distillation of (I). The first was found to be dihydroeugenol (identified by the benzoate), the second, 1-(3,5-dimethoxy-4-hydroxyphenyl)propane (3).


(3)

This substance was obtained in a small quantity by the hydrogenation of maple wood in the presence of Raney nickel by Hibbert and co-workers [6]. It was identified by elementary analysis and the melting point of its acetate which agreed with that given in Hibbert's paper. Therefore, 1-(3,5-dimethoxy-4-hydrophenyl) propane, as well as dihydoreugenol (3) was extracted with ether from the alkaline solution.

EXPERIMENTAL

Preparation of aspen lignin by the copper ammonium method. 1850 g of finely pulverized shavings of freshly cut aspen was extracted 2 times with dichlorethane. The extracted shavings were treated 2 times with 5% aqueous sodium hydroxide solution for 24 hours at room temperature, washed with water, weak acetic acid, again with water, and then boiled with a 1% sulfuric acid solution for 3 hours. The shavings, washed and air dried after this treatment, were shaken for 12 hours with a copper ammonium solution in a bottle filled to the top with the solution. 1500 ml of solution was used for 100 g of shavings. The undissolved part of the wood was pressed free of the solution on a large glass filter (No. 1) and washed first with ammonia, then water, dilute hydrochloric acid, and again with water. The boiling of the residue with 1% sulfuric acid and the shaking with copper ammonium solution was repeated three times. The yield of the lignin was 12%. Found %: C 57.69; H 5.73; OCH_3 20.48.

Treatment of lignin with metallic sodium in liquid ammonia. 15 g of lignin, dried to constant weight over P_2O_5 in a vacuum desiccator, was placed in a reaction vessel, protected from moisture and CO_2 in a Dewar vessel with dry carbon dioxide and acetone. 400 ml of liquid ammonia and 11.25 g of sodium metal in 2 portions, (6 g the first time and 5.25 g on the next day) were added to the vessel. The reaction mixture was mixed daily, and enough liquid ammonia added to replace that lost by evaporation so that the quantity in the vessel was approximately 400 ml. After the decolorization of the solution (7-8 days after the start of the reaction), the ammonia was evaporated, and its remainder swept out by a stream of dry nitrogen and then wet ether was carefully added to the reaction vessel. The reaction mixture was left to stand overnight, and then water was added to the vessel and all of its contents went into solution. The aqueous alkaline solution was extracted with ether. The ether extracts were combined with the ether used for the decomposition of the organo-metallic sodium compounds. The extract, dried over sodium sulfate, was filtered and the ether removed. The residue (0.31 g) was a light yellow oily product (I). The aqueous basic liquid was acidified to Congo with 10% sulfuric acid and extracted together with the residue of the precipitated lignin with ether in a separatory funnel. The ether extracts were dried over sodium sulfate, and the ether was removed. A thick brown syrupy liquid, 2.35 g (II) was obtained.

The unattacked lignin which precipitated upon the acidification of the solution, was filtered, washed with water, and dried first in the air, and then over phosphorus pentoxide in a dessicator; it was a powdered ochre colored substance, 6.79 g (III). The acidic aqueous solution was carefully neutralized to litmus with a sodium hydroxide solution and evaporated in vacuum to a small volume. Upon cooling, absolute alcohol was added to the mixture of crystals and liquid for the precipitation of the sodium sulfate. The mass was left to stand overnight. The salt crystals were filtered and washed with alcohol. The filtrate and the wash alcohol were evaporated to a small volume in vacuum. The liquid was transferred to a small beaker, and the residual alcohol removed in a vacuum desiccator over sulfuric acid. A brown caramel-like substance, 1.7 g (IV), was obtained.

Investigation of (I). 0.6 g of the substance (from two experiments) was redistilled in vacuum at 0.1 mm. Two fractions were obtained: 1) boiling up to 116°, 0.09 g, a yellow transparent liquid; 2) a colorless oily liquid, distilling at 116°, 0.3 g. A benzoate was obtained from the 1st fraction by the Shottenbaumen reaction with m. p. 74° which did not give a depression in a mixed melting point with dihydroeugenol benzoate.

The 2nd fraction gave a crystalline acetate: 0.22 g of the substance, 0.2 g of glacial acetic acid 0.13 g of acetyl chloride were boiled for 1 hour in a small flask with a reflux condenser. The contents of the flask were poured on 2 g of ice. The acetate came out in the form of an oil. It was extracted with ether. The ether extracts were dried with sodium sulfate. After the removal of the ether, the substance crystallized at once. The white crystals which were recrystallized from alcohol melted at 88-89°.

Found %: C 65.37; H 7.64. $C_{13}H_{18}O_4$. Calculated %: C 65.52; H 7.61.

Investigation of (III). The lignin (III) separated by the above method, which was not cleaved to the monomer, was analyzed.

Found %: C 59.43; H 6.10; OCH_3 16.5; OH 15.55.

6 g of the product dried over P_2O_5, was subjected to a second treatment by a solution of metallic sodium in liquid ammonia. The processing of the reaction mass was effected as for the first time. There were obtained: (Ia) 0.06 g (1%), (IIa) 0.33 g (5.5%), and (IIIa) 3.9 g (65%).

(IIIa) was a powder-like substance similar in outer appearance to the starting lignin.

Found %: C 59.44; H 6.10; OCH_3 15.7; OH 15.00.

SUMMARY

1. About 18% of the starting lignin of lower molecular substances, soluble in ether were obtained by the action of a solution of metallic sodium in liquid ammonia on cuprammonium aspen lignin, which is about 2 times greater than the yield of such substances from the fir lignin under the same experimental conditions.

2. 1-(4-Hydroxy-3,5-dimethoxyphenyl) propane and dihydroeugenol were found among the lower molecular weight products of the cleavage.

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* See Consultants Bureau English translation, page 1569

** See Consultants Bureau English translation, page 1243

INVESTIGATION OF GUMBRIN AND ASCANITE AS DEHYDRATING, ISOMERIZING, AND ALKYLATING CONTACT CATALYST

V. ALKYLATION OF ANILINE BY METHYL ALCOHOL IN THE PRESENCE OF GUMBRIN

A. V. Kikvidze and Kh. I. Areshidze

The alkylation of aniline with methyl alcohol in the presence of various catalysts was investigated by E. and K. Smolensky [1]. By repeated passing of the monomethylaniline obtained together with methyl alcohol over Al_2O_3 at 300°, they obtained up to 95% of dimethylaniline. The action of kaoline as a catalyst was found to be analogous to that of Al_2O_3; monomethylaniline was obtained by passing aniline and methyl alcohol over SiO_2 at 300-320°. Brown and Reid [2] investigated the action of silica gel on the alkylation reaction of aniline with methyl, ethyl, n-propyl, and n-butyl alcohols and found that the catalyst shows activity starting at 365°; the reaction product contained olefins and aldehydes in addition to mono- and dialkylanilines. N. I. Shuikin, A. N. Bytkova, and A. F. Ermilina [3] obtained the corresponding monomethyl- and monoethylaniline by the alkylation of aniline with ethyl and methyl alcohols in the presence of the mixed catalyst (Al_2O_3 + Fe_2O_3). The following was reported in the patents [4,5,6]: a) preparation of dimethylaniline by passing a mixture of aniline and methyl alcohol over clay, at 230° ; b) preparation of alkylanilines in the presence of clay, frakonite, silica gel, and others; c) preparation of mono- and dimethylaniline and mono- and diethylaniline by passing the vapors of aniline and dimethyl and diethyl ethers over $Al(OH)_3$ at 220-250° . Certain results are also reported on the alkylation of aromatic hydrocarbons in the presence of activated clay [7]. Gumbrin, as an alkylation catalyst, was studied by Yu. G. Mamedaliev [8]: alkyl benzenes were obtained by the alkylation of benzene with propylene. K. Lavrovsky, A. Mikhnovskaya, and L. Olenchenko [9] investigated the alkylation of aniline with butene in the presence of synthetic alumino-silicates and found that amines, substituted in the ring, are formed as intermediates. The alkylation is accompanied by cracking, destructive alkylation, and cyclization with the formation of p-toluidene as the main reaction product. N. N. Vorozhtsev and I. I. Ioffe [10] obtained p-amylaniline and a mixture of secondary N-alkylanilines by the alkylation of aniline with isopropylethylene in the presence of activated kaolin at 260° and pressures of about 30 atm.

In the present investigation, the action of gumbrin as a catalyst for the alkylation of aniline with methyl alcohol was studied.

EXPERIMENTAL

Freshly distilled aniline (b. p. 182-183° , d_4^{20} 1.0213, n_D^{20} 1.5860) and methyl alcohol (b. p. 65° , d_4^{20} 0.7911, n_D^{20} 1.3231); were used for the experiments. The molecular ratio, methyl alcohol: aniline, 4:1.

As the catalyst, gumbrin in the form of small beads 2-3 mm in diameter initially dried first at room temperature, then in a thermostat at 120-130° , and finally in the reaction tube at the temperature of the reaction was used. The experiments were conducted at 350, 400, and 450°. In each experiment, the mixture of aniline and methyl alcohol was passed uniformly into the reaction tube with a volume velocity of 0.075 liters per liter of catalyst per hour. The reaction product was separated from the water and dried over KOH; the unreacted methyl alcohol was then distilled off. Since it was presupposed that aniline, mono- and dimethylaniline, toluidene, and xylidene were present in the catalyzate, it was treated with phthalic anhydride by means of Porai-Koshits' method [11] to separate dimethylaniline from it. In spite of the fact that the mutual dehydration of aniline and methyl alcohol occurred extensively according to the analytical data, dimethylaniline could not be found. A new method was then used to separate the mixture of primary and secondary amines [12], after its applicability was tested on a synthetic mixture of aniline and monomethylaniline.

As result of the investigation, it was shown that monomethylaniline and a mixture of toluidenes were obtained by the alkylation of aniline by methyl alcohol in the presence of gumbrin (see the Table).

The composition of the mixture in each experiment: aniline 31 g, methyl alcohol, 42.7 g.

According to the boiling point, density, and refractive index, the monomethyl aniline obtained was fairly pure: b. p. 194° (736 mm), n_D^{20} 1.5700; d_4^{20} 0.9885. Literature date: b. p. 193.5° (760 mm), $n_D^{21.2}$ 1.57021; d_4^{20} 0.98912 [13].

	Experiment No.		
	1	2	3
Temperature	350°	400°	450°
Volume velocity of the catalyzing mixture (liters per liter of catalyst per hour).	0.075	0.075	0.075
Yield of monomethylaniline (in %)	37.90	56.02	28.90
Yield of toluidenes (in %). .	5.90	10.40	14.05

SUMMARY

1. The alkylation of aniline with methyl alcohol was first conducted in the presence of gumbrin as a catalyst, and monomethylaniline was obtained in quantities of 37.9, 56.0, and 28.9% at 350, 400, and 450°, respectively.

2. Dimethylaniline was not obtained by the alkylation of aniline with methyl alcohol in the presence of gumbrin.

3. It was also shown that toluidenes were formed, the yields of which were 5.9% at 350°, 10.4% at 400°, and 14.05% at 450°.

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* See Consultants Bureau English translation, page 1821.

SYNTHESIS AND TRANSFORMATION OF CERTAIN DERIVATIVES OF N,N'-DI-(β-HYDROXYETHYL)AMINOACETIC ACID (DIHYDROXYETHYLGLYCOCOL)

I. DEHYDRATION OF DIHYDROXYETHYLAMINOACETIC ACID

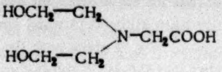
N. V. Khromov and A. Z. Remi ov

The chemistry of morpholine and its derivatives has been very widely developed during the past few years, but compounds with the morpholone ring still remain poorly investigated. N-Methyl- and N-ethylmorpholone were obtained by Knorr [1,2]. Kiprianov and co-workers [3,4,5] synthesized a series of alkyl and aryl morpholones. These papers exhaust the investigations on the morpholone series, so that many of even the simplest members of this series (as for example, morpholone-2) are still unknown up to now. N,N-Di(β-hydroxyethyl)aminoacetic acid is an available source for the synthesis of derivatives of morpholone-2. It was first synthesized by Kiprianov [6] from ethyl glycocolate and ethylene oxide.* As a result of the reaction between the above substances, the formation of nitrogen substituted mono- and dihydroxyethyl derivatives of ethyl glycocolate of the following structure could have been expected:

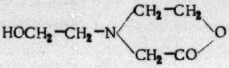
$$HOCH_2CH_2NHCH_2COOC_2H_5 \quad (I) \quad \text{and} \quad (HOCH_2CH_2)_2NCH_2COOC_2H_5 \quad (II).$$

However, neither one of these esters was isolated from the reaction mixture by Kiprianov.

After the corresponding processing of the reaction products, only N,N-di(β-hydroxyethyl) aminoacetic acid (III) was obtained by him, which, as it was shown,-was present in the reaction mixture in the form of the lactone (IV):



(III)



(IV)

The closing of the lactone ring during the reaction of ethyl glycocolate with ethylene oxide occurred, as Kiprianov showed, very easily even when the reaction was effected at room temperature. This revealed the very low stability of the ester of the dihydroxyethyl-derivative (II), which could not be isolated for this reason. The mutual transformations of acid (III) and its lactone (IV) occur without any great difficulty. This acid, upon dry vacuum distillation is transformed into the lactone which is converted, by the evaporation from an aqueous solution, or even in a wet atmosphere, into the starting acid. Kiprianov also showed that both substances are found in equilibrium in aqueous solution, although it is greatly shifted in the direction of the cleavage of the lactone. Only the picrate of acid (III) and the chloroplatinate of its lactone could be obtained by Kiprianov as derivatives of these two compounds. The above lactone (IV) is an N-hydroxyethyl derivative of tetrahydro-2-ketooxazine or morpholone-2.

In the present communication, the synthesis of various derivatives of N,N-di(β-hydroxyethyl) aminoacetic acid, including those containing a morpholone ring, is reported.

The starting dihydroxyethylaminoacetic acid $(HOC_2H_4)_2NCH_2COOH$ was not synthesized according to Kiprianov, but by means of a method developed by the authors, from diethanolamine and monochloroacetic acid.

Such a method for the preparation of dihydroxyethylglycocol is favorably different from that using ethyl oxide because of its simplicity (it does not require that the reaction be conducted under pressure as does Kiprianov's method), and because it gives a final product with a high degree of purity in good yield. By heating the acid obtained to its melting point, its lactone, hydroxyethylmorpholone, was prepared. The picrate and picrolonate, unreported in literature, were obtained from it.

By heating dihydroxyethylglycocol with an excess of hydrochloric acid in vacuum, a salt like compound was obtained which corresponded to the formula $C_6H_{11}NO_3 \cdot HCl$, according to analytical results, which could be assigned the structure of either N-hydroxyethyl morpholine hydrochloride or 4-morpholyl acetic acid hydrochloride. Both of these compounds, being isomers, could have been formed as the result of the dehydration of dihydroxyethylaminoacetic acid by one of the following schemes

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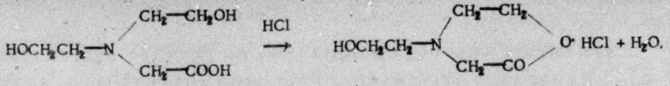
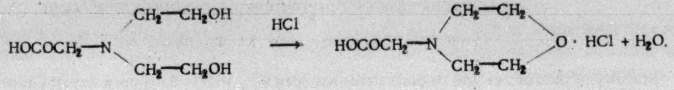
* Later Lyubomudrov [7] obtained dihydroxyethylglycocol from diethanolamine, KCN, and formaldehyde.

1)



2)



Since the physical constants of both hydrochlorides were unknown, and attempts to obtain hydroxyethylmorpholone hydrochloride from the base and hydrogen chloride, in the usual manner in a non-polar solvent, were found to be unsuccessful (hydroxyethylmorpholone is very unstable and, on contact with moisture, more so in the presence of HCl, was rapidly hydrolyzed), the synthesis of morpholylacetic acid hydrochloride, unreported in the literature, was undertaken. It was obtained from morpholine and monochloroacetic acid, and is a white crystalline powder with m. p. 169-170°. Since the hydrochloride of unknown structure obtained from dihydroxyethylglycocol and hydrochloric acid melted at 139-141° and possessed properties differing from morpholylacetic acid hydrochloride (solubility, crystal form, pH of aqueous solution), the structure of N-hydroxyethylmorpholone must be assigned to it. This compound is rapidly hydrolyzed in aqueous solution, and is transformed into dihydroxyethyl glycocol hydrochloride, which results in a drop in the pH of the solution since hydroxyethylmorpholone is a stronger base than dihydroxyethylglycocol. Fig. 1 shows graphically the change of pH with time of a 0.0125 molar hydroxyethylmorpholone hydrochloride solution. In order to prove that, in the above case, the formation of dihydroxyethylglycocol hydrochloride really occurred, the curve of the potentiometric titration of an authentic solution of dihydroxyethylglycocol hydrochloride with 0.1 N alkali was compared with that for the solution of hydroxyethylmorpholone hydrochloride which had initially been allowed to stand until the acidity had achieved a predetermined maximum. Fig. 2 gives both the curves. Their almost complete superimposition shows that the same substances had been titrated in both cases, namely, dihydroxyethylglycocol hydrochloride.

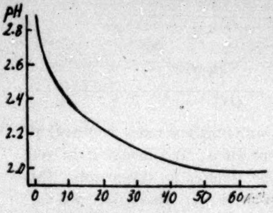
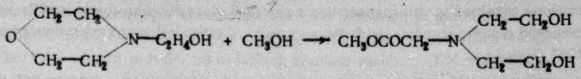


Fig. 1

Both electrolytic dissociation constants were determined for dihydroxyethylaminoacetic acid by potentiometric titration, which, at 19°, were found to be equal to: basic constant, $K_{OH} = 10^{-11.8}$, and acidic constant $K_H = 10^{-8.5}$, or according to Bjorrum, $K_{OH} = 10^{-5.6}$ and $K_H = 10^{-2.3}$.

Interesting properties were found during the preparation of hydroxyethyl morpholone picrolonate. It was a yellow crystalline powder with m. p. 205-206°, very slightly soluble in methanol. However, upon continued heating, this solvent, taken in a quantity not sufficient for complete solution of the substance, gradually went into solution, from which, upon cooling, a voluminous precipitate of a new substance with two melting points formed; initially, it melted at 150-152°, evolving a gaseous product (frothing); then it rapidly solidified and again melted at 203-205°. But, if the capillary with the samples of substance is heated gradually, starting at a temperature not higher than 108-110° then there is no melting at 150-152°, and the substance only melted once, at 203-205°. A mixed melting point of the new substance and the starting hydroxyethylmorpholone picrolonate conducted in this manner, (i.e., gradually heating the capillary) did not give a depression. Therefore, the substance obtained evolved some sort of gaseous product on heating and was transformed into hydroxyethylmorpholone picrolonate. Since it was found that a substance with exactly the same properties (two melting points) was obtained by dissolving dihydroxyethylglycocol in the presence of excess picrolonic acid, it was suggested that it was dihydroxyethylglycocol picrolonate, which loses water on heating and is transformed into hydroxyethylmorpholone hydrochloride. In addition, elementary analysis showed that the compound investigated had an empirical formula of $C_{17}H_{23}N_5O_9$, which differs from that of hydroxyethylmorpholone picrolonate, $C_{16}H_{19}N_5O_8$, by one molecule of methanol, CH_4O. The problem whether or not the methanol was alcohol of crystallization or constitution, was answered simply: the substance did not change both properties after two recrystallizations from acetone (by ether or ethanol), and it was evident that the methanol enters into the composition of the molecule of the substance which must be assigned the structure of methyl dihydroxyethylaminoacetate picrolonate.

Such an ester could have been formed as a result of the alcoholysis of hydroxyethylmorpholone by the reaction:



As had already been found, this type of dihydroxyethylaminoacetic acid esters cannot be isolated in free form since they cyclize quite readily; for this reason it did not appear to be possible to obtain methyl dihydroxyethylaminoacetate picrolonate directly from the ester and picrolonic acid.

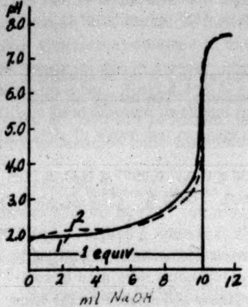


Fig. 2. 1) Hydroxyethylmorpholone hydrochloride; 2) dihydroxyethylglycocol hydrochloride.

In order to prove the correctness of the conclusion on the structure of the new compound, an analogous reaction between hydroxyethylmorpholone picrolonate and ethyl alcohol was performed. In this case, as was expected, ethyl dihydroxyethylaminoacetate picrolonate should have been obtained. Indeed, the substance obtained as a result of such a reaction accurately corresponded in elementary analysis to the desired ethyl dihydroxyethylaminoacetate picrolonate, and also had two melting points. It is of interest that the reaction between hydroxyethylmorpholone picrolonate and alcohols proceeds the more slowly, the more carefully the alcohol is dried; for this reason hydroxyethylmorpholone picrolonate can be recrystallized from anhydrous methanol and ethanol without any risk of contaminating it with alcoholysis products. Conversely, if the alcoholysis is desired, then it is necessary to use wet alcohol, or even to add specially a small amount of water to the reaction mixture, which leads to a considerable increase in the reaction rate.

Such an effect of water on the course of the reaction makes it possible to suppose that the formation of the ester of dihydroxyethylglycocol is preceded by the hydrolysis of hydroxyethyl morpholone, which is completely logical from the properties of this compound. The subsequent esterification of the dihydroxyethylaminoacetic acid formed is catalyzed by the hydrogen atoms, whose source is picrolonic acid. The esterification product, methyl or ethyl dihydroxyethylaminoacetate, unstable in free state, is stabilized by being transformed into the picrolonate.

EXPERIMENTAL

N,N-Di-(β-hydroxyethyl)aminoacetic acid (dihydroxyethylglycocol). 14.1 g (0.15 mole) of monochloroacetic acid was dissolved in 25 ml of water, and neutralized with cooling, (temperature not higher than 30°) with 12 ml of a 50 % NaOH solution until neutral or weakly basic to litmus. The solution of sodium monochloroacetate obtained in this manner was added to 16 g of diethanolamine, and the mixture refluxed until complete disappearance of an alkaline reaction on brilliant yellow paper, which required 3-4 hours. The solution was then evaporated to dryness on the water bath, and the dry residue was boiled with 150 ml of 80% methanol until completely in solution. The solution was filtered hot and left to crystallize. The crystalline mass which precipitated was filtered, washed, first with small amounts of methanol, and then with acetone. Yield 17.5-17.8 g M. p. 179-183°*. The methanol was removed from the mother liquor, and the residue was evaporated on the water bath to completely remove the solvents and to a transformation into a thick crystalline paste, which was then treated with ethanol, sucked in a filter (under vacuum), washed with ethanol and acetone, and dried. The dry powder was boiled with 40-50 ml of 80% methanol, the solution filtered from the residue, and after cooling, 2-3 g of a product with m. p. 175-180° precipitated from it.

The total yield, therefore, was about 20 g or 80-82% of the theoretical. After one recrystallization from 80% methanol, the substance slowly melted at 190-192°, frothing from the separation of water. Because the melting point of dihydroxyethylglycocol was lowered considerably if the sample was kept for a long time at high temperatures, the heating of the capillary with the substance was begun at 180-190°.

N-(β-Hydroxyethyl) morpholone. 5 g of dihydroxyethylglycocol with m. p. 189-192° was placed into a flask of the corresponding size for vacuum distillation. The flask with the substance was placed into a metal bath preheated to 200-210°, and the heating continued until complete cessation of the evolution of water vapor (which could be judged by the complete stopping of frothing), but no more than 12-15 minutes. The flask was then cooled somewhat, fitted with stoppers (with capillary and thermometer) connected to the vacuum, and its contents distilled, collecting a fraction boiling at 162-164° at 3 mm. Yield 3.8-4.0 g or 85-90% of the theoretical. The hydroxyethylmorpholone obtained in this manner was a colorless glycerine-like liquid readily soluble in water and in all of the common organic solvents, with the exception of ether and saturated hydrocarbons. B. p. 163° (3mm), 168° (4 mm), 174° (5 mm).

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* Here and in other parts of the text, the temperature is corrected for the exposed mercury column.

N-Hydroxyethylmorpholone picrate. 1.2 g of hydroxyethylmorpholone was dissolved in 2-3 ml of absolute benzene and mixed with a hot solution of 1.9 g of picric acid in 10 ml of absolute benzene. The orange oil which separated, crystallized on standing. The picrate, recrystallized from absolute alcohol, melted at 136-138°. It was readily soluble in acetone and glacial acetic acid. It was insignificantly soluble in water and other common solvents.

0.2154 g substance; 0.3052 g CO_2; 0.0750 g H_2O. 0.2494 g substance; 0.3536 g CO_2; 0.0877 g H_2O. 0.1205 g substance; 15.9 ml N_2 (21°, 754 mm). 0.1167 g substance; 15.1 ml N_2 (20°, 751 mm). Found %: C 38.67, 38.69; H 3.89, 3.93; N 15.20, 14.90. $C_{12}H_{14}N_4O_{10}$. Calculated %: C 38.50; H 3.77; N 14.97.

N-Hydroxyethylmorpholone picrolonate. It was prepared by mixing a hot concentrated solution of picrolonic acid (in absolute alcohol) and a benzene solution of hydroxyethylmorpholone. Both components were used in equimolecular ratio. The precipitated crystalline residue was separated from the mother liquor and washed on the filter with a small amount of alcohol, and then with ether. The substance, recrystallized from dry methanol, was a dark yellow crystalline powder (under the microscope long well formed prisms) with m. p. 205-206° (with decomposition), very soluble in acetone and glacial acetic acid, slightly in water and the lower alcohols (in the cold), and insoluble in ether and hydrocarbons.

0.2404 g substance; 0.4152 g CO_2; 0.1068 g H_2O. 0.1399 g substance: 0.2438 g CO_2; 0.0613 g H_2O. 0.0975 g substance; 14.7 ml N_2 (20°, 752 mm). 0.1084 g substance: 16.0 ml N_2 (20°, 752 mm). Found %: C 47.13, 47.45; H 4.97, 4.90; N 17.38, 17.01. $C_{16}H_{19}N_5O_8$. Calculated %: C 46.95; H 4.68; N 17.11.

Methyl dihydroxyethylaminoacetate picrolonate. 10 g of hydroxyethylmorpholone picrolonate was refluxed in a small flask with 8-12 ml of methanol to which 0.3-0.5 ml of water was added (to accelerate the reaction). After 3-5 minutes, everything dissolved. The heating was continued for 5-7 minutes more, and the almost completely transparent solution was left to crystallize. The methyl dihydroxyethylaminoacetate which formed, separated in the form of bright yellow, well formed, long needles, which were frequently visible to the naked eye. The substance crystallized very well from methanol, and had two melting points. First it melted at 150-152°, frothed, and rapidly solidified. Upon further heating, the second melting point occurred at 203-205° (with decomposition). If the capillary with the sample was heated gradually starting with a temperature below 100-120°, then the substance melted only once, i. e. at 203-205°. The compound retained all of its characteristic properties after recrystallization from acetone by ether, ethanol by acetone. Methyl dihydroxyethyl aminoacetate picrolonate was also obtained by dissolving dihydroxyethylaminoglycocol in boiling methanol solution of picrolonic acid.

0.1443 g substance: 0.2464 g CO_2; 0.0704 g H_2O. 0.1696 g substance; 0.2886 g CO_2; 0.0805 g H_2O. 0.1220 g substance: 16.8 ml N_2 (24°, 768 mm). 0.1147 g substance; 15.9 ml N_2 (24°, 774 mm). Found %: C 46.60, 46.44; H 5.46 5.31; N 15.99, 16.23. $C_{17}H_{23}N_5O_9$. Calculated %: C 46.26; H 5.25; N 15.86.

Ethyl NN-dihydroxyethylaminoacetate ethyl dihydroxyglycocolate picrolonate. 1.0 g of N-hydroxyethylmorpholone picrolonate was boiled (in a test tube with reflux condenser) with 8 ml of ethanol to which 0.5-0.7 ml of water had been added (to accelerate the reaction). After 8-10 minutes, the residue dissolved completely. The boiling was continued for 5-7 minutes more, and the residue was then allowed to crystallize. The precipitated crystals were separated from the mother liquor and washed with benzene and ether. The product obtained in this manner consisted of a mixture of the starting hydroxyethylmorpholone picrolonate and ethyl dihydroxyethylamino acetate picrolonate. Both of these substances are not very different from each other in solubility and crystallizing properties. However, after a long series of fractional crystallizations from absolute alcohol, ethyl dihydroxyethylamino acetate picrolonate was obtained in almost pure form and was in the form of bright yellow long thin needles collected into starlike aggregates. The substance, like the analogous methyl ester, melted first at 138-139° (upon heating the sample starting at 130-132°), then rapidly solidified and melted once more at 202-204° (with decomp.). On the gradual heating of the capillary with the sample starting below 120-130°: the substance melted only once, namely, at 202-204°.

0.1260 g substance: 0.2204 g CO_2; 0.0631 g H_2O. 0.1348 g substance: 0.2348 g CO_2; 0.0658 g H_2O. 0.1052 g substance: 14.5 ml N_2 (24°, 748 mm). 0.0893 g substance; 12.3 ml N_2 (26°, 754 mm). Found %: C 47.73, 47.50; H 5.60 5.46; N 15.59; 15.60. $C_{18}H_{25}N_5O_9$. Calculated %: C 47.47; H 5.53; N 15.38.

N-Hydroxyethylmorpholone hydrochloride. 5 g of dihydroxyethyl glycocol was dissolved in 5 ml of C. P. hydrochloric acid (d. 1.19), and the solution obtained evaporated in vacuum starting at the temperature of boiling water. and finally at 130-140° (on a glycerine bath). The reaction was stopped when the formation of gas bubbles ceased in the layer of the thick, transparent liquid. After cooling, the semi-solid, amorphous mass (resembling red glue in surface appearance) obtained in this manner was treated with 6-7 ml of boiling absolute alcohol. The crystalline residue, poorly soluble in alcohol formed in this manner, was filtered and washed, first with small amounts of acetone, and then with ether. Yield 4.3-4.5 g or 78-80% of the theoretical. The substance was a white crystalline powder which crystallized from absolute methanol in the form of colorless prisms with sharp angles with m. p. 139-141°; it was readily soluble in water, hot methanol, and glacial acetic acid. Its solubility in all other common solvents is very small.

0.1761 g substance: 0.2568 g CO_2; 0.1072 g H_2O. 0.1823 g substance: 0.2624 g CO_2; 0.1112 g H_2O. 0.3438 g substance: 23.2 ml N_2 (23°, 752 mm). 0.2164 g substance: 14.45 ml N_2 (21°, 746 mm). 0.1768 g substance: 0.1409 g AgCl. 0.1440 g substance; 0.1138 g AgCl. Found %: C 39.80, 39.28; H 6.81, 6.83; N 7.70, 7.88; Cl 19.72, 19.55. $C_6H_{12}NO_3Cl$. Calculated %: C 39.68; H 6.66; N 7.71; Cl 19.53.

Potentiometric measurements. The potentiometric determination here reported were effected with a vacuum tube GIPKh potentiometric systemwith glass electrodes and calomel polyelement as the electrode with the standard potential. The characteristics of the glass electrode were determined graphically by points obtained by the registration of the millivoltmeter readings of the potentiometer while the electrodes were immersed in a buffer solution with an accurately established pH. The characteristic line of the glass electrode constructed in this manner, with sufficient accuracy corresponded to the equation:

$$y = 0.115x + 0.10,$$

where y is the pH of the solution, x, the reading of the apparatus (mV);

Observation of the change of pH of the solution of N-hydroxyethylmorpholone hydrochloride with time. A sample of 0.1815 g (0.001 mole) of hydroxyethylmorpholone hydrochloride was dissolved in 80 ml of double distilled water. The potentiometric measurement of the hydrogen ion concentration was made for the 0.0125 molar solution, prepared in this way, over a determined interval of time.

The results obtained are given in Table 1.

TABLE 1

Time (in min.)	Reading (in mV)	pH of solution	Time (in min.)	Reading (in mV)	pH of solution
0	24.5	2.9	14	19	2.3
2	22.5	2.7	23	18	2.15
4	22	2.6	45	16.5	2.0
5	21	2.5	65	16.5	2.0
8	20	2.4	-	-	-

As is apparent from the results in Table 1, the acidity of the solutions of hydroxyethylmorpholone hydrochloride increase quite rapidly with time, which was related to the hydrolysis of hydroxyethyl morpholone to form dihydroxyethylaminoacetic acid.

Potentiometric titration of hydroxyethylmorpholone hydrochloride with 0.1 N NaOH solution. After the prepared 0.0125 molar solution of hydroxyethylmorpholone hydrochloride had stopped changing its pH (see above), it was titrated potentiometrically with 0.1 N NaOH. The results of the titration are given in Table 2.

Potentiometric titration of a solution of dihydroxyethylaminoacetic (dihydroxyethylglycocol) hydrochloride. An 0.0125 molar solution of dihydroxyethylaminoacetic acid hydrochloride (0.163 g of the acid, 10 ml of 0.1N HCl. 70 ml of water) was prepared and titrated potentiometrically. The results are given in Table 3.

As is shown by comparison of the results of titrations of the solution of hydroxyethylmorpholone hydrochloride and dihydroxyethylglycocol hydrochloride (Table 2 and 3), the same substance was titrated in both cases, namely, dihydroxyethylglycocol hydrochloride.

Therefore, hydroxyethylmorpholone hydrochloride is transformed in aqueous solutions to the same salt of dihydroxyethylglycocol.

Determination of the ionization constants of N,N-dihydroxyethylaminoacetic acid. The determination of the ionization constants (acidic and basic) of dihydroxyethylaminoacetic acid was made by means of the pH at the half equivalent points in one case by titration with acid, and in the other with base. For the determination of the acidic ionization constant, 5 ml of exactly 0.1 N NaOH was added to 50 ml of an 0.02 molar solution of dihydroxyethylaminoacetic acid and the pH was measured (at 19°). It was found to be equal to 8.5. Therefore, the apparent constant of acidic ionization was equal to $10^{-8.5}$ at the above temperature. For the analogous determination of the basic ionization constant, a solution of the amino acid containing exactly 0.001 mole in 70 ml was prepared. After the addition of exactly 5.0 ml of exactly 0.1 N HCl, the pH of the solution was found to be equal to 2.3. Since the measurement was effected at 19°, and since the ion product of water at this temperature is equal to $10^{-14.1}$, the apparent basic ionization constant (basicity constant) of dihydroxyethylaminoacetic acid is equal to $10^{-11.8}$. The true constants (according to Bjorrum) must, therefore, be equal to the acidic, $10^{-2.3}$, and basic, $10^{-5.6}$.

TABLE 2

0.1 N NaOH (in ml)	Reading (in mV)	pH
0.0	16.5	2.0
5.0	19.0	2.3
9.0	26.5	3.2
9.2	27.0	3.2
9.4	29.0	3.4
9.6	30.0	3.55
9.8	32.0	3.8
9.9	36.5	4.3
10.15	47	5.5
10.25	57	6.6
10.45	60	7.0
10.7	62	7.2
11.0	64	7.4
11.5	66	7.7
12.0	68	7.9

TABLE 3

0.1 N NaOH (in ml)	Reading (in mV)	pH
0.0	15.5	1.9
0.5	17.0	2.1
2.0	17.5	2.1
3.0	18.0	2.2
5.0	19.0	2.3
7.0	21.0	2.5
8.0	22.0	2.6
8.5	23.0	2.7
9.0	25.0	3.0
9.5	27.0	3.2
9.75	29.0	3.4
9.95	38.0	4.5
10.2	54.0	6.3
10.45	60.0	7.0
11.0	64	7.4
11.45	65.5	7.6

SUMMARY

1. It was shown that N-hydroxyethylmorpholone hydrochloride is formed by the dehydration of N,N-di-(β-hydroxyethyl) aminoacetic acid hydrochloride.

2. A series of new derivatives of N-hydroxyethylmorpholone was synthesized: picrate, picrolonate, hydrochloride, and their properties were studied.

3. It was shown that hydroxyethylmorpholone picrolonate is readily transformed into the corresponding methyl and ethyl dihydroxyethylaminoacetate picrolonates by treatment with methanol or ethanol. This series of esters is unknown in the free form, and this is the first preparation of their picrolonates. The role of water is this reaction was explained.

4. The electrolytic dissociation constants of dihydroxyethylglycocol were determined.

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ON THE QUESTION OF THE PREPARATION OF p-NITROTRIPHENYLAMINES

P. M. Bugai

Various methods [1] are encountered in the literature for the preparation of 4-nitrotriphenylamine, 4,4'-dinitrotriphenylamine, and 4,4',4"-trinitrotriphenylamine wherein each substance is obtained separately under defined conditions. Using Heydrich's method [2,3] for the preparation of 4-nitrotriphenylamine, this product could not be obtained in perceptible amount. It was shown that dinitro- and trinitrotriphenylamine were formed under the given conditions. On charging 2 g of triphenylamine and 24 g of glacial acetic acid into a flask, only part of the triphenylamine dissolves. Then on introducing gradually 4 g of a nitrating mixture (consisting of 6 parts by weight of fuming nitric acid, d 1.49, and 10 parts by weight of glacial acetic acid), an excess of nitric acid is created, and the reaction favors the formation of dinitro- and trinitrotriphenylamine, since the undissolved part of the triphenylamine does not take part in the nitration reaction.

To prove this assumption, the following method was used: immediately after the addition of all of the nitrating mixture, the residue of the triphenylamine was filtered and once more dissolved in 24 g of glacial acetic acid to complete solution, and up to 2 g of the nitrating mixture was added. The heating conditions were those recommended in the method, i.e., 45-50°.

As a result of this experiment, a mixture of dinitro- and trinitrotriphenylamine was obtained from the first half of the triphenylamine, where there was an excess of the nitrating mixture, and almost exclusively mononitrotriphenylamine from the second part, where an additional amount of glacial acetic acid was used to dissolve the triphenylamine completely, and half the amount of the nitrating mixture was added. Starting from the impossibility of obtaining all three of the above nitro derivatives of triphenylamine, a method for the combined preparation of these compounds was arrived at. In this method, triphenylamine is used completely, and all three substances are obtained.

For the separation of the nitro derivatives of triphenylamine, their properties of dissolving in different concentrations of acetic acid on heating was used. 4-Nitrotriphenylamine dissolves in 50% acetic acid on boiling and crystallizes in the cold: 4,4'-dinitrotriphenylamine dissolves in 80% acetic acid on boiling and precipitates on cooling; these substance precipitate out more completely if the acetic acid solution is poured into water; 4,4',4"-trinitrotriphenylamine does not dissolve in concentrated acetic acid, nor even in boiling glacial acetic acid. Therefore, mononitrotriphenylamine is extracted from the mixture by heating with 50% acetic acid. The residue is then treated with boiling 80% acetic acid which is removed from the residue remaining, which is nothing less than trinitrotriphenylamine. The latter is once more heated in glacial acetic acid for the complete removal of the remaining other derivatives of triphenylamine. This is also a method for the purification of 4,4',4"-trinitrotriphenylamine. 4-Nitrotriphenylamine and 4,4'-dinitrotriphenylamine were repeatedly recrystallized from the same solutions of acetic acid with which they were extracted.

The substances obtained had the following characteristics: 4-nitrotriphenylamine, m.p. 138-139°, 4,4'-dinitrotriphenylamine, m.p. 206-207°, 4,4',4"-trinitrotriphenylamine, m.p. 279-280° which correspond to the literature results.

The practical yields of the nitro derivatives are: the mononitroderivative, up to 20-25%, dinitroderivative up to 30%, and the trinitroderivative, up to 40%.

SUMMARY

1. One method was used for the preparation of all three p-nitroderivatives of triphenylamine instead of the three different ones reported in the literature.

2. By using the combination method, and the different solubility of the nitro derivatives of triphenylamine in dilute solutions of acetic acid, all three substances were obtained separately in quite pure state.

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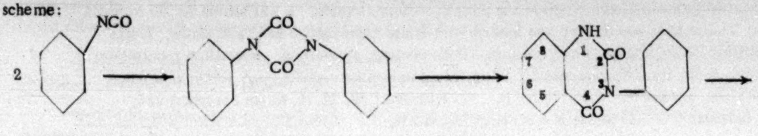
INVESTIGATION OF ORGANIC ISOCYANATES

I. TRANSFORMATIONS OF THE ISOCYANATES OF THE BENZENE SERIES BY THE ACTION OF ALUMINUM CHLORIDE

N. S. Dokunikhin and L. A. Gaeva

Organic isocyanates with aromatic hydrocarbons, in the presence of aluminum chloride, form substituted amides of the aromatic carboxylic acids. According to Leucart [1] the process occurs via a stage of the addition of the elements of hydrogen chloride to the isocyanate molecule, and analogously to the preparation of unsubstituted aromatic carboxylic acid amides by the action of chlorocarbamic acid [2], is a partial case of acylation according to Friedel-Crafts.

Previously the transformations of aromatic isocyanates without the participation of aromatic hydrocarbons by the action of aluminum chloride had been briefly reported [3]. Salts of amino carboxylic acids can be obtained by the alkaline processing of the reaction products. Isocyanates of the benzene series give only o-aminocarboxylic acids in this case. It was suggested that the process occurs by the intermediate formation of dimeric isocyanates. On further investigation, it was shown that the substances obtained by the reaction of the isocyanates of the benzene series or their dimers with molten aluminum chloride are: 3-phenyl-2,4-dioxotetrahydroquinazoline and its corresponding derivatives. The process can be described by the following scheme:

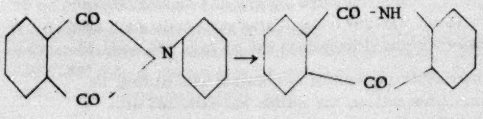


(I) (II) (III)

$\longrightarrow o\text{-}C_6H_4NH_2COOH + C_6H_5NH_2$

(IV) (V)

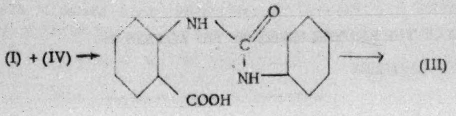
The transformation of the dimer of phenylisocyanate (II) into 3-phenyl-2,4-dioxotetrahydroquinazoline is analogous to the known isomerization of phthalanil (VI) in molten aluminum chloride, also leading to an expansion of the ring, and the entrance of the substituent into the o-position to the amino group [4] (VIII).



(VI) (VII)

The structure of the transformation products of phenyl isocyanate and its dimer (III) was proved by its identification with the substance obtained by a reported method [5] from phenyl isocyanate and anthranilic acid, followed by ring closure with hydrogen chloride in ethyl alcohol medium.

The transformation into quinazoline and o-aminocarboxylic acid derivative was studied with the following: phenyl isocyanate, o-, m-, and p-tolyl isocyanate, xylyl isocyanate, 4-diphenyl isocyanate, o-, m-, and p-chlorophenyl isocyanate, and 2,5-dichlorophenylisocyanate, as well as dimers of these compounds.



The quinazoline derivative was not isolated in pure form with 4-diphenyl isocyanate, but was directly transformed into 4-aminodiphenyl-3-carboxylic acid. For m-substituted phenyl isocyanates, where the formation of two isomers was possible, only quinazoline and anthranilic acid derivatives with the carboxylic acid groups in the p-position to the chloro or methyl group were isolated.

Outside of 3-chloroanthranilic acid, the o-aminocarboxylic acids obtained correspond in properties to those reported in the literature. There is a substance listed by this name in the "Encyclopedia of Organic Compounds " [6] with m.p. 148°, obtained by Hübner and Weiss [7] from 3-chlorobenzoic acid by nitration and reduction, which was assigned the above structure by Eller and Klemm without sufficient basis [8]. The acid obtained from 2-chlorophenyl isocyanate had an m.p. 190.6-191.2°. Removal of the amino group by the action of nitrogen oxides in alcoholic solution results in the formation of 3-chlorobenzoic acid, corresponding in its properties to that reported in the literature, and identical to the one obtained in an analogous manner from 5-chloroanthranilic acid. With the presence of a fixed o-positioned Cl and amino group in the starting substance, as well as an o-positioned amino and carboxylic acid group in the derived dioxotetrahydroquinazoline, there is no doubt of the structure of the substance isolated.

EXPERIMENTAL

3-Phenyl-2,4-dioxotetrahydroquinazoline. 1) 12 g of phenyl isocyanate was introduced at 135-140° into a melt obtained from 97 g of aluminum chloride and 23 g of sodium chloride. It was stirred for 30 minutes and poured on ice. The residue was filtered and washed with dilute hydrochloric acid and water. It was extracted with a boiling 2% sodium carbonate solution. Upon cooling, a colorless, crystalline precipitate came out. The yield of the dry substance was 5.9 g (49.2%). Lancet-like crystals from acetic acid m.p. 280-281.4 (278-280° [9]). Found: C 70.53, 70.30; H 4.27, 4.02; N 11.58, 11.78, M (in camphor) 237, 244. $C_{14}H_{10}O_2N_2$. Calculated %: C 70.58; H 4.23; N 11.76; M 238.

2) 30 g of freshly distilled phenyl isocyanate and 5 g of anhydrous pyridine were allowed to stand for three days at room temperature. The coarse rhombic crystals of phenyl isocyanate dimer which formed, were filtered, washed with benzene, and recrystallized from benzene: m.p. 175.2-176° (175-176° [10]).

9 g of phenyl isocyanate dimer was introduced into a molten mixture of 72.5 g of aluminum chloride and 17.5 g of sodium chloride at 135-140°, stirred for 30 minutes, and then processed as in the previous experiment. 5.79 g (64.3%) of 3-phenyl-2,4-dioxotetrahydroquinazoline was obtained.

3) 3 g of 2-carboxy-N,N'-diphenylurea (m.p. 182.8-183°), obtained by the reaction of phenyl isocyanate with sodium anthranilate, was placed into 15 ml of ethyl alcohol, and a stream of hydrogen chloride passed in, first at room temperature, and then with heating. On cooling, the precipitated 3-phenyl-2,4-dioxotetrahydroquinazoline was filtered. 1.94 g of the substance was obtained; m.p. 281.0-282.0° after recrystallization from acetic acid. A mixed sample with the substance obtained from phenyl isocyanate had an m.p. 280.0-281.6°.

2-Aminobenzoic acid. 4 g of 3-phenyl-2,4-dioxotetrahydroquinazoline was heated, with stirring, for 6 hours with 50 ml of a 10% potassium hydroxide solution. Upon cooling, the aniline was extracted with benzene, and 1.78 g of anthranilic acid with m.p. 145.0-146.2° (from water) was obtained on acidification to pH 3.5-4.0.

3-(2'-Tolyl)-8-methyl-2,4-dioxotetrahydroquinazoline. o-Tolyl isocyanate (b.p. 184-186°) was obtained by the action of phosgene on o-toluidine hydrochloride.

1.44 g (24%) of 3(2'-tolyl)-8-methyl-2,4-dioxotetrahydroquinazoline with m.p. 225-227° (from glacial acetic acid) was obtained from 6 g of o-tolyl isocyanate under the conditions of the experiment with phenyl isocyanate.

Found %: C 71.74, 71.83; H 5.45, 5.63; N 10.09, 10.17. $C_{16}H_{14}N_2O_2$. Calculated %: C 72.18; H 5.26; N 10.52.

2-Amino-3-methylbenzoic acid. 0.2 g (71.4%) of the substance was obtained from 0.5 g of 3(2'-tolyl)-8-methyl-2,4-dioxotetrahydroquinazoline. Prisms from water with m.p. 170.8-172.2° (172° [6]).

3-(3'-Tolyl)-7-methyl-2,4-dioxotetrahydroquinazoline. 10 g of m-tolyl isocyanate (b.p. 187.2-187.4°), prepared by the action of phosgene on molten m-toluidine hydrochloride, was introduced into a molten mixture of 80 g of aluminum chloride and sodium chloride at 135°. It was stirred for 30 minutes and poured into ice and water. It was filtered, washed with dilute acid and water. The residue was mixed at room temperature with a 5% potassium hydroxide solution. It was filtered and 3-(3'-tolyl)-7-methyl-2,4-dioxotetrahydroquinazoline was precipitated from the filtrate with hydrochloric acid. Yield 5.08 g (50.8%). Platelets from isobutanol. M.p. 290.5-292.5°.

Found %: C 72.55, 72.15; H 5.73, 5.44; N 10.09, 10.16. $C_{16}H_{14}N_2O_2$. Calculated %: C 72.18; H 5.26; N 10.52.

2-Amino-4-methylbenzoic acid. 0.91 g (70%) of the substance with m.p. 176.0-177.2° (177° [6]) was obtained from 2.3 g of 3-(3'-tolyl)-7-methyl-2,4-dioxotetrahydroquinazoline.

3-(4'-Tolyl)-6-methyl-2,4-dioxotetrahydroquinazoline. 1) 3.6 g (44%) of 3-(4'-tolyl)-6-methyl-2,4-dioxotetrahydroquinazoline was obtained from 8.05 g of p-tolyl isocyanate (b.p. 187-189°) prepared by the action of phosgene in 1-chloronaphthalene on p-toluidine hydrochloride. Platelets from ethyl alcohol; m.p. 288-290° (with decomposition).

Found %: C 72.36, 72.63; H 5.68, 5.55; N 10.71, 10.61. $C_{16}H_{14}N_2O_2$. Calculated %: C 72.18; H 5.26; N 10.52.

2) 1.0 g (50%) of a substance identical with 3-(4'-tolyl)-6-methyl-2,4-dioxotetrahydroquinazoline synthesized from p-tolyl isocyanate, was obtained from p-tolyl isocyanate dimer, prepared from a mixture of pyridine and p-tolyl isocyanate by allowing it to stand for 20 days.

2-Amino-5-methylbenzoic acid. 0.45 g (44.2%) of the substance was obtained from 1.8 g of 3-(4'-tolyl)-6-methyl-2,4-dioxotetrahydroquinazoline. Platelets from aqueous methyl alcohol; m.p. 173.8-174.8° (175° [6]).

3-(2'-Chlorophenyl)-8-chloro-2,4-dioxotetrahydroquinazoline. 2-Chlorophenyl isocyanate (b.p. 200-203°) was prepared by the action of phosgene on molten 2,2'-dichloro-N,N'-diphenylurea.

3.6 g of 3-(2'-chlorophenyl)-8-chloro-2,4-dioxotetrahydroquinazoline (48.1%) was obtained from 7.48 g of o-chlorophenyl isocyanate. Platelets from ethyl alcohol with m.p. 223.0-224.0°: b.p. 223.0-224.0°. Found %: C 54.09; 54.39; H 2.69, 2.76; Cl 23.34, 23.71. $C_{14}H_8N_2O_2Cl_2$. Calculated %: C 54.72; H 2.61. Cl 23.12.

3-Chloroanthranilic acid. 1.48 g (88%) of 3-chloroanthranilic acid was obtained from 3.0 g of 3-(2'-chlorophenyl)-8-chloro-2,4-dioxotetrahydroquinazoline. Curved needles from water; m.p. 190.6-191.2°. Found %: C 48.35-48.34; H 3.56, 3.77; N 8.35, 8.42; Cl 20.20, 20.01. $C_7H_6O_2NCl$. Calculated %: C 48.97; H 3.49; N 8.16; Cl 20.69.

A stream of nitrogen oxides was passed into a boiling solution of 0.2 g of 3-chloroanthranilic acid in 20 ml of ethyl alcohol. It was diluted with 20 ml of water, and sodium hydroxide added to the strongly alkaline reaction mass. It was heated to saponify the ethyl chlorobenzoate, evaporated to half the volume, and filtered. 3-Chlorobenzoic acid was isolated from the filtrate by acidification. Colorless needles from water. M.p. 154-156° (158° [6]). It did not give a depression in melting point with the substance obtained by an analogous method from 5-chloroanthranilic acid.

3-(3'-Chlorophenyl)-7-chloro-2,4-dioxotetrahydroquinazoline, m-Chlorophenyl isocyanate (b.p. 200.0-203.5°) was obtained by the action of phosgene on molten 3,3'-N,N'-diphenylurea. 4.9 g (46.6%) of 3-(3'-chlorophenyl)-7-chloro-2,4-dioxotetrahydroquinazoline was obtained from 10.5 g of m-chlorophenyl isocyanate. Needles from glacial acetic acid. M.p. 309.5-311.0°.

Found %: C 54.72, 54.44; H 2.66, 2.64; N 9.93, 9.81; Cl 22.23, 23.37. $C_{14}H_8N_2O_2Cl_2$. Calculated %: C 54.72; H 2.61; N 9.12, Cl 23.12.

4-Chloroanthranilic acid. 0.9 g of 4-chloroanthranilic acid (81%) was obtained from 2 g of 3-(3'-chlorophenyl)

-7-chloro-2, 4-dioxotetrahydroquinazoline. Needles from aqueous ethyl alcohol; m.p. 238.5-239.5° (240° [6]).

3-(4'-Chlorophenyl)-6-chloro-2,4-dioxotetrahydroquinazoline. p-Chlorophenyl isocyanate (b.p. 203-204°, m.p. 32.5°) was obtained by the action of phosgene on molten 4,4'-dichlorodiphenylurea. 2.42 g (48.4%) of the substance was obtained from 5 g of p-chlorophenyl isocyanate. Needles from glacial acetic acid; m.p. 323.5-325.0°.

Found %: C 54.50, 54.63; H 2.85, 2.60; N 9.91, 9.93; Cl 22.93, 22.95. $C_{14}H_8N_2O_2Cl_2$. Calculated %: C 54.72; H 2.61; N 9.12; Cl 23.12.

The dimer of p-chlorophenyl isocyanate was formed by storing a mixture of it with pyridine. Six-faceted platelets from chloroform. It resists heating to 160-170°, does not melt, and does not have a pure melting point. 2.17 g of 3-(4'-chlorophenyl)-6-chloro-2,4-dioxotetrahydroquinazoline (62%), identical with that obtained from the monomeric isocyanate, was obtained from 3.5 g of the dimer.

5-Chloroanthranilic acid. 2.3 g (78%) of 5-chloroanthranilic acid was obtained from 5.3 g of 3-(4'-chlorophenyl)-6-chloro-2,4-dioxotetrahydroquinazoline. Needles from water; m.p. 210.0-210.5° (211-212° [6]).

3-(2',5'-Dichlorophenyl)-5,8-dichloro-2,4-dioxotetrahydroquinazoline. 2,5-Dichlorophenyl isocyanate was obtained by the action of phosgene on molten 2,5-dichloroacetanilide. B.p. 233.0-233.5°, m.p. 27.4-28.8°. Curved needles from carbon tetrachloride.

The reaction with aluminum chloride was conducted at 155-160°. 2.47 g (41.2%) of 3-(2',5'-dichlorophenyl)-5,8-dichloro-2,4-dioxotetrahydroquinazoline was obtained from 6 g of the isocyanate. Rectangular platelets from isobutanol: m.p. 281.8-283.0°.

Found %: C 44.27, 44.29; H 1.96, 1.78; Cl 38.45, 38.78. $C_{14}H_6N_2O_2Cl_4$. Calculated %: C 44.68; H 1.59; Cl 37.76.

3,6-Dichloroanthranilic acid. 6 g of 2,5-dichlorophenyl isocyanate was melted with aluminum chloride and sodium chloride at 155-160°. After pouring on ice, filtering, and washing free of mineral salts, the residue was boiled with stirring for 6 hours with 35 ml 10% potassium hydroxide solution. It was filtered, and the filtrate was acidified with hydrochloric acid to pH 2.5. The precipitated 3,6-dichloroanthranilic acid was filtered, washed, and dried. Yield 1.6 g (48.6%). Needles from water. M.p. 152.8-154.0° (154-155° [6]).

3-(2',4'-Dimethylphenyl)-6,8-dimethyl-2,4-dioxotetrahydroquinazoline. 2,4-Xylyl isocyanate (b.p. 211.2-212.0°) was obtained by the action of phosgene on molten acetylxylidine. 2.28 g (22.8%) of 3-(2',4'-dimethylphenyl)-6,8-dimethyl-2,4-dioxotetrahydroquinazoline was obtained from 10 g of xylyl isocyanate. Prisms from isobutanol; m.p. 253.0-254.5°.

Found %: N 9.41, 9.35. $C_{14}H_{18}O_2N_2$. Calculated %: 9.52.

2-Amino-3,5-dimethylbenzoic acid (4-aminomesitylenic acid). 0.32 g (12.3%) of 4-aminomesitylenic acid was obtained from 4 g of 2,4-xylyl isocyanate. M.p. 189.6-190.8° (191° [6]).

2-Amino-5-phenylbenzoic acid (4-aminodiphenyl-3-carboxylic acid). 4-Diphenyl isocyanate (m.p. 55.5°) was obtained by the action of phosgene on 4-aminodiphenyl hydrochloride in toluene.

10 g of the isocyanate was introduced into a molten mixture of 80 g of aluminum chloride and 20 g of sodium chloride at 135-140°. It was stirred for 30 minutes, the reaction mixture poured on ice, filtered, washed to complete removal of the mineral salts. The residue was boiled with 100 ml of a 10% sodium hydroxide solution and filtered. The residue was once more treated with a sodium hydroxide solution. The combined filtrates were acidified with hydrochloric acid to pH 4. The precipitated 2-amino-4-phenylbenzoic acid was filtered, washed with water, and dried. Yield 3.57 g (65.5%). Plates or needles from aqueous ethyl alcohol. M.p. 202.6-203.8° (201-202° [11]).

Found %: C 73.35, 73.14; H 5.37, 5.32; N 6.72, 6.79. $C_{13}H_{11}O_2N$. Calculated %: C 73.22; H 5.20; N 6.57.

SUMMARY

1. It was shown that 3-phenyl-2,4-dioxotetrahydroquinazoline and its derivatives were formed by the reaction of isocyanates of the benzene series with a molten mixture of aluminum chloride and sodium chloride. These are split into the corresponding aromatic amine and salt of the o-aminobenzoic acid upon heating with

solutions of alkalies. The reaction was investigated on examples of chloro-, methyl-, and phenyl derivatives of phenyl isocyanate.

2. The reaction can be used for preparative purposes for the introduction of a carboxylic acid group into the benzene ring in an o-position to the amino group. The o-aminocarboxylic acids formed are free from isomers. In the case of m-chloro and methyl derivatives, the carboxylic group enters into the p- position to the above substituent.

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INVESTIGATIONS OF ALKANESULFONIC ACIDS

VII. REACTIONS OF ALKANESULFONYL CHLORIDES WITH p-AMINOPHENOLS

A. G. Kostsova

The reactions of alkanesulfonyl chlorides with p-aminophenol ethers, p-anisidine and p-phenetidine [1] were studied and reported by the authors. The present investigation was concerned with the study of the reaction of alkanesulfonyl chlorides and p-aminophenol itself. These reactions are only known for aromatic sulfonyl chlorides [2].

Recently, a reaction between p-aminophenol and methanesulfonyl chloride has been reported in the literature [3]. The authors used for their experiments with p-aminophenol methane-, ethane-, 2-methylethane-, butane-, and 2-methylbutanesulfonyl chlorides. Three substances can be obtained from this reaction:

$RSO_2NHC_6H_4OH$ (I) $NH_2C_6H_4OSO_2R$ (II) $RSO_2NHC_6H_4OSO_2R$ (III)

It was necessary to find out which one of the three possible compounds was formed during these reactions, or whether or not all of them are formed simultaneously. The reactions were mainly conducted in acetone with heating. During these reactions, noticeable tarring occurred especially with 2-methylethanesulfonyl chloride, the reaction product of which could not be isolated in pure form. In all of the other cases only one product was isolated from sulfonyl chloride. According to the empirical composition, they correspond to products (I) and (II). But elementary analysis does not allow the question of which one of these two compounds is actually formed in these reactions to be answered, since they are both isomers, and therefore, are identical in empirical composition. In order to determine which structure to assign to the compounds isolated, p-hydroxyalkanesulfoanilides (I), or p-aminophenylalkane sulfonates (III), a series of characterizing reactions were made. Thus the isonitrile test for the free NH_2 group was done. The formation of an isonitrile was not found at the moment of the reaction, nor upon standing, which showed that the free NH_2 group was absent. In order to test for the ester, the product was boiled with dilute alkali. The cooled alkaline solution was acidified with dilute acid. The unchanged product with the same melting point precipitated. If the ester had been present, it would have been hydrolyzed, since sulfonic acid esters are easily hydrolyzed, not only by alkalies, but also by boiling with water.

Therefore, these characteristic reactions, supplemented by the quantitative analysis, lead to the conclusion that the reaction of alkane sulfonyl chlorides with p-aminophenol under the above conditions leads to formation of only p-hydroxyalkanesulfoanilides see Table), and the compounds obtained have the general formula (I). Esters, as well as products of structure (III), are not formed in these cases.

Expt. No.	Formula	Name	Melting Point
1	$CH_3CO_2NHC_6H_4OH$	p-Hydroxymethanesulfoanilide	156°
2	$CH_3CH_2SO_2NHC_6H_4OH$	p-Hydroxyethanesulfoanilide	113
3	$CH_3CH_2CH_2CH_2SO_2NHC_6H_4OH$	p-Hydroxybutanesuloanilide	84
4	$(CH_3)_2CHCH_2CH_2SO_2NHC_6H_4OH$	p-Hydroxy(2-methyl)butanesulofanilide	88

EXPERIMENTAL*

The starting p-aminophenol was obtained from its hydrochloride by treatment with sodium carbonate, M.p. 183°. The sulfonyl chlorides were prepared by the usual methods [4]. A whole series of experiments was conducted to study the reaction of the alkane sulfonyl chlorides with p-aminophenol; these experiments were effected under equal conditions and with different quantitative ratios of the reactants. Only the most typical of the experiments conducted are reported in the experimental section.

1. Reaction of methanesulfonyl chloride with p-aminophenol. 3.82 g of p-aminophenol was dissolved in 50 ml of acetone. 2 g of methanesulfonyl chloride was added dropwise to the solution. The reaction was conducted on a water bath heated to 80° under reflux for 1-1.5 hours. The mixture browned strongly. The hydrochloride of p-aminophenol precipitated. At the end of the reaction, the mixture was cooled, the salt separated, washed with acetone, and dried. M.p. over 200° with decomposition. The salt was not investigated

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* N. N. Khrunin, G. F. Titova, and V. I. Sergeeva participated in the experimental section.

any further. The acetone was either evaporated, or distilled from the filtrate. A dark thick oil remained as a residue. Upon standing, the oil solidified. The crude tarry reaction product was treated with animal charcoal in boiling water. The aqueous extract was separated from the charcoal (hot filtration) and cooled. Rose-gray crystals of p-hydroxymethanesulfoanilide separated. Yield 2.45 g or 50% of the theoretical. The product is readily soluble in acetone, alcohol, ether, poorly in benzene and water. The experiment reported was conducted with 1 mole of the sulfonyl chloride for 2 moles of p-aminophenol. When the reaction was conducted with a molar ratio of 1:1, the yield of the product decreased noticeably.

0.1010 g substance: 5.30 ml 0.1 N H_2SO_4. 0.1102 g substance: 0.1370 g $BaSO_4$. Found %: N 7.34; S 17.04. $C_7H_9O_3NS$. Calculated %: N 7.48; S 17.11.

2. Reaction of ethanesulfonyl chloride with p-aminophenol. 3 g of ethanesulfonyl chloride, 5.08 g of p-aminophenol were dissolved in 60 ml of acetone. The reaction was then conducted analogously to the previous one. The reaction product was in the form of greyish white crystals. Yield 2.25 g or 48% of the theoretical. Conducting the reaction without heating, decreases the yield of the product to 40-41%. The solubility of the product was analogous to the previous one.

0.1082 g substance: 5.30 ml 0.1 NH_2SO_4. 0.1213 g substance: 0.1408 g $BaSO_4$. Found %: N 6.86; S 15.91; $C_8H_{11}O_3NS$. Calculated %: N 6.96; S 15.92.

3. Reaction of 2-methylethanesulfonyl chloride with p-aminophenol. Different quantitative ratios of the reactants (1:1, 1:2), different solvents (acetone, alcohol, pyridine), different reaction temperatures all led to the same result, to a strongly tarred grease-like product from which the pure reaction product could not be isolated.

4. Reaction of butanesulfonyl chloride with p-aminophenol. 3 g of butanesulfonyl chloride and 4 g of p-aminophenol were dissolved in 45 ml of acetone. The reaction conditions and the isolation of the product were analogous to the previous ones. 0.7 g or 16% of the theoretical of pure p-hydroxybutanesulfoanilide was isolated from the strongly tarred product. Still lower yields resulted if the reaction was conducted under other conditions, because of considerably more tarring. The solubility of the product was analogous to the previous.

0.0626 g substance: 2.75 ml 0.1 N H_2SO_4. 0.1022 g substance: 0.1025 g $BaSO_4$. Found %: N 6.15; S 13.75. $C_{10}H_{15}O_3NS$. Calculated %: N 6.11; S 13.97.

5. Reaction of 2-methylbutanesulfonyl chloride and p-aminophenol. 2 g of 2-methylbutanesulfonyl chloride and 2.6 g of p-aminophenol were dissolved in 50 ml of acetone. The reaction conditions, and the isolation of the product were analogous to the previous. The yield of pure p-hydroxy(2-methyl) butanesulfoanilide was 0.68 g or 25% of the theoretical. Greyish-white leaflets. A yield of 30-33% was obtained when the reaction was conducted in absolute alcohol. In this case, p-aminophenol hydrochloride did not precipitate, as it was soluble in alcohol. The alcohol was distilled, and a dark thick oil remained as the residue which solidified on cooling. The solid residue, which was a mixture of p-hydroxy-(2-methyl) butanesulfoanilide and p-amino phenol hydrochloride, was treated with boiling water; the salt remained in solution, and the p-hydroxy (2-methyl) butanesulfoanilide came out from the solution on cooling in the form of yellow-grey crystals, readily soluble in acetone, alcohol and ether, and poorly in benzene and water.

0.0566 g substance: 2.32 ml 0.1 N H_2SO_4. 0.1019 g substance: 0.0988 g $BaSO_4$. Found %: N 5.7; S 13.29. $C_{11}H_{17}O_3NS$. Calculated %: N 5.76; S 13.17

SUMMARY

1. The reaction between alkanesulfonyl chlorides and p-aminophenol was studied under various conditions.
2. p-Hydroxymethane-, ethane-, butane-, (2-methyl) butanesulfoanilides were obtained and characterized.

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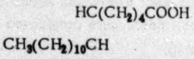
* See Consultants Bureau English translation, page 1471.

REACTIVITY OF PETROSELIC AND PETROSELAIDIC ACIDS AND THEIR ESTERS

A. K. Plisov and A. I. Bykovets

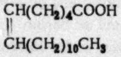
One of the authors has recently reported on the reactivity of oleic and elaidic acids and their esters [1]. It was found that their chemical reactivity was in complete correlation with the theory of steric hinderance. In this communication, the analogous question in relation to petroselic acid and its stereo isomer, petroselaidic acid, is discussed. Petroselaidic acid has been known for a relatively long time; however, the question of its spatial configuration has not been solved by chemical means up to now.

Petroselic acid with m. p. 33-34° is assigned the cis-configuration, whereas its isomer with m.p. 54°, petroselaidic acid—the trans,by analogy to the fact that, in these cases, generally, the lower melting form corresponds to the cis-configuration, and that melting at a higher temperature, the trans, even though now there are cases known which do not correspond to this rule.



$$\begin{array}{r} HC(CH_2)_4COOH \\ CH_3(CH_2)_{10}CH \end{array}$$

petroselaidic acid



$$\begin{array}{l} CH(CH_2)_4COOH \\ \| \\ CH(CH_2)_{10}CH_3 \end{array}$$

petroselic acid

The question of the actual configuration of petroselic and petroselaidic acids can be answered to considerable extent by chemical means if it is considered that an analogous effect of the radicals at the double bond on their reactivity occurs, as in the case of oleic acid.

The oxidation, hydrogenation, and saponification reactions of petroselic and petroselaidic acids and their methyl, propyl, and benzyl esters were studied. It was found that petroselic acid and its esters were oxidized and hydrogenated more easily than petroselaidic acid and its esters, but the saponification of petroselates proceeds more slowly than that of the petroselaidates. All of these facts favor the cis configuration for petroselic acid and the trans configuration for petroselaidic acid.

EXPERIMENTAL

Petroselic acid was isolated from the fatty oil of coriander, and purified by distillation at 216-218°/8-9 mm. Crude petroselaidic acid was obtained by the isomerization of petroselic acid in the presence of HNO_2. After recrystallization from alcohol, the petroselaidic acid had an m.p. 52-54°.

Methyl, propyl, and benzylic esters of these acids were prepared by heating a mixture of the alcohol and the acid on a water bath in the presence of H_2SO_4. Methyl petroselate, purified by distillation at 2-3 mm, had a b.p. 158-160°, methyl petroselaidate, b.p. 164-165°. Propyl petroselate distilled at 198-200° at 4-5 mm, propyl petroselaidate, at 200° (2 mm).

The benzyl esters had not been reported in the literature.

Benzyl petroselate, a light yellow liquid with a weak esterlike odor, dissolved in five parts of ethanol at room temperature, boiled in vacuum (1 mm) at 218°. d_4^{23} 0 9315, n_D^{20} 1.4825.

Benzyl petroselaidate, a light yellow, almost without odor, dissolved at 40° in five parts of alcohol, and upon cooling below room temperature, rapidly crystallized into a white mass of needles. It boils in vacuum (2-3 mm) at 229°. d_4^{20} 0.9372, n_D^{23} 1.4842.

The determination of the rate of saponification of the methyl esters was effected in the same manner as was described in more detail for the experiments with oleic acid [1]. Two identical samples of the isomeric esters (1/2000 of a mole) were weighed into vessels for measuring conductance, 21 ml alcohol was added to dissolve the ester, and then 2 ml of 0.1 N alcoholic KOH solution. All of the experiments were conducted in a thermostat at 23°. The moment of addition of the alkali was considered the start of each experiment. In each repeat experiment, the vessel for measuring conductance was changed, and in this way, the sample of the cis isomer, was placed first in one vessel, and then in the other in which the trans isomer was found in the first experiment. The measurement of the electroconductivity was conducted by means of a resistance bridge and a vacuum tube resistance indicator.

TABLE 1

Decrease in the Electroconductivity (in % of the initial) upon Saponification of the Esters of Petroselic and Petroselaidic Acids in 2.5 Hours

Ester	Expt. 1	Expt. 2
Methyl petroselate	11	11
Methyl petroselaidate	16	16
Propyl petroselate	10	–
Propyl petroselaidate	16	–
Benzyl petroselate	8.1	8.0
Benzyl petroselaidate	16	16

Table 1 gives the results of the determination of the electroconductivity of the mixtures of the esters and the alkali.

If the data on the percent change in the electroconductivity in each pair of the experiments for the two isomers are compared, then it is found that in all cases the petroselates are saponified more slowly than the petroselaidates. In addition, it was observed that the benzyl group has the greatest effect in this respect.

The hydrogenation of petroselic and petroselaidic acids and their esters was accomplished in alcoholic solutions in the presence of platinum deposited on barium sulfate. The experiments were conducted in a "goose," simultaneously with two identically weighed samples of the isomers, at 23° (Table 2).

TABLE 2

Hydrogenation time (in min.)	Amount of hydrogen added (in ml)							
	petroselic acid	petroselaidic acid	methyl petroselate	methyl petroselaidate	propyl petroselate	propyl petroselaidate	benzyl petroselate	benzyl petroselaidate
20	30	26	30	24	30	24	14	16
40	60	46	58	40	55	42	35	27
60	78	66	80	66	80	67	80	31

The oxidation of petroselic and petroselaidic acids and their esters was accomplished with an aqueous solution of $KMnO_4$. The course of the oxidation reaction was judged by the change of the electroconductivity of the aqueous $KMnO_4$ solution, the electroconductivity of which changed gradually with the consumption for the oxidation. The conductance increases since the KOH appears instead of $KMnO_4$, which possess a higher conductance.

The oxidation was conducted in a thermostat simultaneously with an identical sample of the isomer (1/1500 of a mole) in identical vessels with platinum electrodes. 5 ml of a 1.5 % $KMnO_4$ solution was used (Table 3).

The results in Tables 2 and 3 are little different from those of analogous experiments with oleic and elaidic acids and their esters; in all cases the same thing occurred, petroselic acid and its esters are oxidized and hydrogenated more rapidly than petroselaidic acid and its esters. The benzyl group has a considerably greater decelerating effect on the oxidation of petroselaidates than the methyl.

The difference in the oxidizability of petroselic and petroselaidic acids or their esters can be observed visually, if equal quantities of the isomers and a weakly colored $KMnO_4$ solution are placed in identical cylinders. A noticeable change in the color soon appears in one of the cylinders, with equal shaking; then the solution in this cylinder decolorizes, whereas at the same time, there is still a noticeable color in the other cylinder. This experiment can be recommended for a lecture demonstration of the different reactivities of the isomeric acids and their esters, or their derivatives.

TABLE 3

Increase in the Electroconductivity (in % of the initial) upon the Oxidation of Petroselic and Petroselaidic Acids and Their Esters for 45 Minutes by Permanganate

Acid or ester	Temp. (in °)	Change in electroconductivity (in %)
Petroselic acid	55	39
Petroselaidic acid	55	26
Methyl petroselate	24	23
Methyl petroselaidate . . .	24	15
Propyl petroselate	24	24
Propyl petroselaidate	24	15
Benzyl petroselate	26	23
Benzyl petroselaidate	26	12

SUMMARY

1. It was shown that petroselic and petroselaidic acids and their esters show different reactivities. Petroselic acid and its esters are oxidized and hydrogenated more rapidly than petroselaidic acid and its esters, while the saponification of the petroselates proceeds more slowly than that of

the petroselaidates.

2. The reactions studied confirmed the cis-configuration of petroselic acid and the trans-configuration of petroselaidic acid.

3. The benzyl esters of petroselic and petroselaidic acids were synthesized, and their properties reported.

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* See Consultants Bureau Translation, p. 69.

REACTIONS OF AN ACTIVE AMINO GROUP

II. DISPLACEMENT OF THE AMINO GROUP IN β-DIALKYLAMINOPROPIONITRILE

A. P. Terentyev, A. N. Kost, and S. M. Gurvich

It is known that the amino group in β-amino ketones, β-aminoacids, and compounds analogous to them possesses a great ability for displacement.

In the present communication the ability of the amino group in β-dialkylaminopropionitriles for displacement was investigated. Previously it was shown by the authors [1] that the dialkylamino group in these compounds is capable of a series of displacement reactions, but that these processes proceeded comparatively slowly. For this reason the reactivity of quaternary ammonium salts obtained from β-dialkylaminopropionitriles was investigated.

It was found that these quaternary salts of these bases split off acrylonitrile on pyrolysis; in the presence of alkalies the process occurs readily even at 100°.

$$XR_3NCH_2CH_2CN \rightarrow R_3N + HX + CH_2{=}CH{-}CN.$$

Since acrylonitrile was obtained readily and in good yield with this method, it appeared to be of preparative interest. Thus, acrylonitrile was obtained in a 75-80% yield by heating β-chloropropionitrile and triethylamine in the presence of an equivalent amount of alkali.

$$ClCH_2CH_2CN \xrightarrow{(C_2H_5)_3N + KOH} CH_2{=}CH{-}CN.$$

Because the tertiary amine is not consumed during the reaction (it is lost only by being removed with the water vapor and the acrylonitrile), it can be used in comparatively small quantity in the reaction.

The amino group could be exchanged by an alkoxyl residue by the action of methyl or butyl alcohol (in the presence of alkali) on the quaternary salt:

$$CH_3OH + XR_3NCH_2CH_2CN \rightarrow CH_3OCH_2CH_2CN.$$

Judging by the easy removal of the acrylonitrile group in alkaline media, it could also be assumed that in the above case the process of displacement of the amino occurs by means of a stage of the formation of acrylonitrile. This completely agrees with the experiments on transcyanoethylation [2].

The change to a methyl group occurs with poor yield as a result, apparently, of the low boiling point of the alcohol.

Heating β-diethylaminopropionitrile methiodide with an aqueous solution of potassium cyanide gave succinic acid in good yield.

$$KCN + ICH_3(C_2H_5)_2NCH_2CH_2CN + H_2O \rightarrow HOOCCH_2CH_2COOH.$$

Therefore, the above quaternary salts are capable of various exchange reactions, similar to those which occur with the leucotrope's O or with gramine.

β-Dimethylaminopropionitrile and β-diethylaminopropionitrile were chosen as the aminotriles, and were obtained by the usual methods, i.e., by the action of acrylonitrile on the corresponding amine [3]. β-Chloropropionitrile was obtained by passing hydrogen chloride into acrylonitrile [4].

EXPERIMENTAL

Pyrolysis of the dimethyl sulfate salt of β-dimethylaminopropionitrile. The salt was obtained by the slow addition of freshly distilled dimethyl sulfate to a benzene solution of an equimolar amount of β-dimethylaminopropionitrile. Colorless needles from methyl alcohol.

10 g of this salt was heated on a metal bath in a Favorsky flask equipped with two thermometers (in the vapor and in the reaction mass). At 120° a slow decomposition of the substance began with the formation of acrylonitrile and trimethylamine. A 200° the reaction proceeded energetically, and at 240°, foaming and partial tarring occurred. 1.7 g of acrylonitrile was collected as a result of the pyrolysis, i.e., 70% of the theoretical.

Pyrolysis of the dimethyl sulfate salt of β-diethylaminopropionitrile. The pyrolysis was conducted analogously to the previous one. The cleavage of the salt began at 180° and proceeded exothermically (the temperature of mixture spontaneously rose to 200°). Upon heating to 240°, a violent decomposition occurred with frothing. 4.7 g of a liquid distilling at 69-74° was obtained from 20 g (about 0.08 mole). After drying with potassium carbonate, and fractionally distilling, 0.4 g of methyldiethylamine was isolated. B.p. 66-69°; picrate, m.p. 184°, (from alcohol).

Literature data: b.p. 66-67° [5]; picrate, m.p. 183-185° [6].

In addition, 3.6 g of acrylonitrile (i.e., 86% of the theoretical) was obtained.

If the pyrolysis was conducted in the presence of alkali, the cleavage began at 100°. Thus 2.9 g of acrylonitrile i.e., 88% of the theoretical, was obtained from 15.8 g (about 0.06 mole) of the salt by heating it to 100-200°, in the presence of 0.5 g (about 0.01 mole) of solid potassium hydroxide.

Preparation of acrylonitrile from β-chloropropionitrile. A flask equipped with a dropping funnel and dephlegmator was placed into a bath heated to 120°, and a mixture of 28 g (0.5 mole) of potassium hydroxide and 10 g (about 0.1 mole) of triethylamine placed into the flask. Then 44.9 g (0.5 mole) of β-chloropropionitrile was added dropwise at such a rate that the thermometer in the dephlegmator registered not higher than 80°. The distilled acrylonitrile was acidified with dilute hydrochloric acid, washed once with ice water (5 ml), dried with calcium chloride, redistilled, dried with potassium carbonate, and once more redistilled. 20-22 g of acrylonitrile was obtained, i.e. 75-80% of the theoretical. B.p. 77-78°.

Substitution by a methoxy group. 22 g (0.1 mole) of the dimethyl sulfate salt of β-dimethylaminopropionitrile was added to the alcoholate obtained from the solution of 4.6 g (0.2 g-atom) of sodium in 60 ml of absolute methyl alcohol. The mixture was heated to reflux for 4 hours on the water bath, whereby the separation of trimethylamine occurred. The excess methyl alcohol was then removed in vacuum, the residue was diluted with water, acidified with hydrochloric acid, and extracted 4 times with ether. The ether solution was dried with fused magnesium sulfate and distilled. 1.8 g of β-methoxypropionitrile was obtained, i.e. 21% of the theoretical calculated on the dimethyl sulfate salt. B.p. 164-165° at 765 mm: d_4^{20} 0.9488; n_D^{20} 1.4031; MR_D 21.89; calculated 22.13, which corresponds to the literature data [7].

Substitution by a butoxy group. 24.0 g (0.1 mole) of β-dimethylaminopropionitrile methiodide was added to a warm solution of 5.6 g (0.1 mole) of potassium hydroxide in 74 g (1 mole) of absolute butyl alcohol. The mixture was heated to reflux until the evolution of trimethylamine ceased (about 6 hours), then it was acidified to Congo with hydrochloric acid, and water was added until solution of the precipitated salts. The alcoholic layer was separated, washed twice with small portions of ice water, dried over sodium sulfate, and vacuum distilled. 10.1 g (73.7 % of the theoretical) of β-butoxypropionitrile was obtained. B.p. 80-82° at 10 mm, d_4^{20} 0.8904; n_D^{20} 1.4174 MR_D 35.95; calculated 35.99. Literature data: b.p. 98 at 20 mm, d_{20}^{20} 0.8863; n_D^{20} 1.4180 [7].

Reaction with potassium cyanide. A mixture of 13.4 g (0.05 mole) of β-diethylaminopropionitrile methiodide [4], 4.8 g (about 0.06 mole) of 85% potassium cyanide, and 50 ml of water was heated for 6 hours in a steel autoclave to 150-160°. The mixture was cooled, filtered from a small amount of a residue, carefully acidified with sulfuric acid, and extracted many times with ether. After evaporation of the ether and recrystallization from water, 4.7 g (i.e., 80% of the theoretical) of succinic acid was obtained. M.p. 182°, which corresponds to the literature data.

SUMMARY

1. It has been shown that the amino group in the quaternary salts of β-dialkylaminopionitriles can be substituted by various residues.

2. A new method for the preparation of acrylonitrile is reported.

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• See Consultants Bureau English translation, page 2027.

SULFONATION AND SULFONIC ACIDS OF ACIDOPHOBIC COMPOUNDS

XXIII. SULFONATION OF ALDEHYDES AND KETONES

A. P. Terentyev and L. A. Yanovskaya

In addition to the heterocycles of the furan, pyrrole, and thiophene group, and conjugated dienic hydrocarbons, etc., there exist other groups of acidophobic compounds. One of the most important and widely distributed of these are the aliphatic, fatty aromatic, and alicyclic aldehydes and ketones. Most of them are very sensitive to the usual sulfonating agents, as for example, strong sulfuric acid, chlorosulfonic acid, etc. The reaction with such agents leads, as a rule, not to sulfonation, but to condensation, polymerization, or oxidation of the carbonyl compound. It is not surprising that there are only individual cases of the direct sulfonation of ketones, and especially aldehydes.

Thus, by the action of 50% oleum on acetaldehyde, propionaldehyde, and acetone, in addition to the decomposition products, disulfoacetaldehyde, disulfopropionaldehyde, and trisulfoacetone were obtained [1]. 15% oleum sulfonates acetone in acetic anhydride solution to ω-sulfoacetophenone [2]. Recently, a paper was published on the sulfonation of certain aldehydes (isobutyraldehyde, heptaldehyde, and phenylacetaldehyde) and ketones (acetone, pinacoline, and a series of aryl aliphatic ketones) by means of dioxane sulfotrioxide [3]. Finally, papers are known on the sulfonation of complex alicyclic ketones with chlorosulfonic acid [4]; especially well studied is the sulfonation of camphor [5].

In the present communication the results of the investigation of the sulfonation of aldehydes and ketones with various sulfonating agents is reported: solution of sulfur trioxide in dichlorethane, pyridine sulfotrioxide, pyridine bisulfotrioxide, and dioxane sulfotrioxide. Several results of this investigation have already been published in the form of a preliminary communication [6].

As was mentioned above, sulfonation products can be obtained by the action of oleum on certain aldehydes and ketones, even though the process is accompanied by strong tarring and the decomposition of the carbonyl compounds. It was decided to investigate the action of a dilute solution of sulfur trioxide in dichlorethane on aldehydes and ketones. It was found that a sulfur trioxide dichlorethane solution acts upon propionaldehyde and diisopropyl ketone at room temperature to produce tars: upon the introduction of the carbonyl compound into the solution of the sulfonating agent (or in reverse order), a strong heating occurs and the solution darkens, the odor of sulfur dioxide is detected, and finally, a dark viscous mass separates. After the usual processing of the reaction mixture obtained with an aqueous suspension of barium carbonate, it is possible to isolate a small amount of a dark barium salt of the sulfonic acid.

If the reaction is conducted as follows: the sulfur trioxide is added slowly to the solution of the carbonyl compound with strong cooling and stirring, the darkening is moderated; sometimes the odor of sulfur dioxide is noticed at the end of the reaction. In this case, the barium salts of monosulfopropionaldehyde and monosulfodiisopropyl ketone were isolated in the usual manner in yields of 35-40% and 70-75%, respectively. However, especially in the case of the aldehyde, the salts were contaminated by side products.

The successful application of heterocyclic acidophobic compounds pyridinesulfotrioxide [7] and dioxanesulfotrioxide [8] stimulated the authors to try these reagents for the sulfonation of aldehydes and ketones. As was found experimentally, pyridinesulfotrioxide is poorly suited as a sulfonating agent for aldehydes and ketones. The sulfonation reaction only starts at higher temperatures (100-140°), and it is complicated by considerable polymerization and tarring of the carbonyl compound. In a series of cases (diisopropyl ketone) the reaction practically did not occur. The yields of the sulfonic acids (isolated in the form of barium salts by the usual method) were always very small (15-20%). Therefore, pyridinesulfotrioxide was found to be insufficiently active as an agent for the sulfonation of the carbonyl compound. For this reason, we tested the action on aldehydes and ketones (propionaldehyde and diisopropyl ketone) of pyridinebisulfotrioxide, which was found by one of the authors [9] to be a more energetic sulfonating agent. Pyridinebisulfotrioxide, formed by reaction of an equimolecular amount of pyridinesulfotrioxide and sulfur trioxide, acts on solutions of carbonyl compounds in dichlorethane even at room temperature. Diisopropyl ketone forms the monosulfonic acid readily and in good (80-85%) yield. Propionaldehyde gives either the disulfonic acid, or a mixture of mono- and disulfonic acids; the pure monosulfonic acid could not be obtained.

Finally, dioxanesulfotrioxide was tried as a sulfonating agent for carbonyl compounds. The method of sulfonation with this compound was practically the same for all cases: the aldehyde or ketone was added directly to a suspension or solution (in an excess of dioxane) with efficient cooling and stirring. Solution of the dioxanesulfotrioxide (in the case of a suspension) and an insignificant warming of the mixture occurred. The solution obtained was allowed to stand for 12 hours at room temperature, then processed, and the barium salt of the sulfonic acid was isolated in the usual manner. In certain cases the sulfonation was effected in reverse order, i.e., a solution of the dioxanesulfotrioxide was added to a solution of the aldehyde or the ketone.

By using dioxanesulfotrioxide, in relation to the amount of the reagent used, both the mono- and disulfonic acids of aldehydes and ketones can be readily obtained. Especially easily formed are the disulfonic acids of aldehydes and ketones. Acetaldehyde, propionaldehyde, butyraldehyde, isobutyraldehyde, isovaleraldehyde, heptaldehyde, octaldehyde, and decylaldehyde, as well as phenylacetaldehyde, acetone, diisopropyl ketone, dipropyl ketone, acetophenone, and cyclohexanone were sulfonated.

It must be mentioned that the method of sulfonation developed by the authors was used by A. N. Nesmeyanov and co-workers [10] for the sulfonation of 7-methylspiro-(4,5)-decan-6-one, 2,2,6-trimethylcyclohexanone, and camphenilone. In the first two cases, the corresponding sulfonic acids in yields of 88 and 90% were obtained in the form of the barium salts. Camphenilone was not sulfonated under the above conditions.

The structure of phenylacetaldehyde and acetophenone sulfonic acids was proved by the oxidation of their barium salts to benzoic acid with potassium permanganate. The α-position of the sulfo group in sulfobutyraldehyde and sulfoheptaldehyde was proved by their oxidation with chromic mixture to acetic and valeric acid respectively, which were isolated and identified in the form of the silver salts; the α- and α',α-positions of the sulfogroups in sulfodipropyl ketone and disulfodipropyl ketone were proved by the oxidation of corresponding barium salts to propionic acid.

All of the barium salts of the sulfoaldehydes and sulfoketones, with the exception of acetophenone sulfonic acid, were readily soluble in water. The majority of them crystallize with one molecule of water which is held quite stably by the salt. Aldehydosulfonic acids give the silver mirror reaction and reduce Fehling's solution, however they do not color fuchsine sulfurous acid. The oximes, phenylhydrazones, and semicarbazones of the aldehydo- and ketosulfonic acids could not be obtained by the usual methods. Benzylthiouronium salts were prepared from the barium salts of the aldehydo- and ketosulfonic acids; however those of the aldehydosulfonic acids were found to be oily liquids and unsuitable for characterization. Sulfoketones gave crystalline benzylthiouronium salts with sharp melting points. The barium salt of sulfobutyraldehyde was converted to sodium and potassium salt by treatment with the corresponding sulfates: white crystalline substances readily soluble in water.

EXPERIMENTAL

Sulfonation of acetaldehyde. A solution of dioxane sulfotrioxide, prepared from 6.6 g of sulfur trioxide in 25 ml of dichlorethane and an excess of acetone, was added slowly with efficient cooling and stirring to a solution of 5.6 g of acetaldehyde in 10 ml of dichlorethane. The mixture was kept for 12 hours at 0°, treated with an aqueous barium carbonate suspension to a neutral reaction, the mixture evaporated to dryness, and the residue extracted with boiling water. The extract was evaporated and the salt was precipitated with a mixture of alcohol and ether. 6.5 g of the salt (39% calculated on the sulfur trioxide) was obtained.

11.750 mg substance: 6.889 mg $BaSO_4$. 8.120 mg substance: 4.738 mg $BaSO_4$. Found %: Ba 34.50, 34.34. $(C_2H_3O_4S)_2 \cdot Ba \cdot H_2O$. Calculated %: Ba 34.20.

8.8 g of acetaldehyde was added at 0° to a suspension of dioxanesulfotrioxide prepared from 35 g of sulfur trioxide in dichlorethane. After 12 hours, the sulfonic acid was isolated in the form of the barium salt by the usual method. 49 g of the salt was obtained (quantitative yield of the disulfonic acid).

7.320 mg substance: 4.720 mg $BaSO_4$. 7.457 mg substance: 4.790 mg $BaSO_4$. Found %: Ba 37.94, 37.80. $C_2H_2O_7S_2Ba \cdot H_2O$. Calculated %: Ba 38.42.

Sulfonation of propionaldehyde. A solution of 8 g of sulfur trioxide in 20 ml of dichlorethane was added slowly with good cooling and stirring to a solution of 5.8 g of propionaldehyde in 20 ml of dichlorethane. The darkening of the solution and the weak odor of sulfur dioxide was noticed. The mixture was treated directly with an aqueous suspension of barium carbonate. 7 g of the salt was obtained in the usual manner. After 3 recrystallizations from a water-alcohol mixture, an analytically pure sample of the salt was obtained:

6.350 mg substance: 3.442 mg $BaSO_4$. Found %: Ba 31.90. $(C_3H_5O_4S)_2Ba \cdot H_2O$. Calculated %: Ba 31.98.

8.5 g of propionaldehyde was added with cooling by ice water to pyridinebisulfotrioxide prepared from 24 g of pyridinesulfotrioxide and 12 g of sulfur trioxide in 40 ml of dichlorethane. A slight darkening and small amount of heating occurred. After usual processing, 12.5 g of the barium salt was obtained.

4.140 mg substance: 2.726 mg $BaSO_4$. 2.847 mg substance: 1.859 mg $BaSO_4$. Found %: Ba 38.76, 38.43. $C_3H_4O_7S_2Ba$. Calculated %: Ba 38.87.

Dioxanesulfotrioxide from 9 g of sulfur trioxide in 25 ml of dichlorethane was added to a solution of 6 g of propionaldehyde, with cooling and stirring. After 12 hours, it was processed in the usual manner. 11.5 g of the salt (55%) was obtained.

8.750 mg substance: 4.743 mg $BaSO_4$. 6.850 mg substance: 3.173 mg $BaSO_4$. Found %: Ba 31.90, 31.73. $(C_3H_5O_4S)_2Ba \cdot H_2O$. Calculated %: Ba 31.90.

Sulfonation of butyraldehyde. 7.2 g of butyraldehyde was added with cooling and stirring to a suspension of dioxanesulfotrioxide in dichloroethane prepared from 8.7 g of sulfur trioxide. After 12 hours, 13.4 g of the barium salt (61%) was obtained with the usual processing.

6.640 mg substance: 3.357 mg $BaSO_4$. 6.690 mg substance: 3.390 mg $BaSO_4$. Found %: Ba 29.75, 29.89. $(C_4H_7O_4S)_2Ba \cdot H_2O$. Calculated %: Ba 30.01.

The sodium salt of sulfobutyraldehyde was prepared by the accurate precipitation of a solution of the barium salt with sodium sulfate.

5.132 mg substance: 2.132 mg Na_2SO_4. 8.475 mg substance: 3.539 mg Na_2SO_4. Found %: Na 13.45, 13.52. $C_4H_7O_4Na$. Calculated %: Na 13.20.

5 g of the barium salt of sulfobutyraldehyde was oxidized by heating for 50 minutes on the water bath with a solution of chromic anhydride in conc. sulfuric acid (slightly greater than the calculated amount). The mixture obtained was diluted with water, and the acetic acid was steam distilled and isolated from the distillate in the form of the silver salt.

8.340 mg substance: 5.381 mg Ag. 9.117 mg substance: 5.889 mg Ag. Found %: Ag 64.61, 64.59. $C_2H_3O_2Ag$. Calculated %: Ag 64.64.

Sulfonation of isobutyraldehyde. 8 g of isobutyraldehyde was added with cooling and stirring to a suspension of dioxanesulfotrioxide in dichlorethane prepared from 10 g of sulfur trioxide. After 12 hours, 17 g (75%) of the barium salt was obtained in the usual manner.

6.890 mg substance: 3.455 mg $BaSO_4$. 9.300 mg substance: 4.680 mg $BaSO_4$. Found %: Ba 29.51, 29.61. $(C_4H_7O_4S)_2Ba \cdot H_2O$. Calculated %: Ba 30.01.

Sulfonation of isovaleraldehyde. The sulfonation of isovaleraldehyde was effected in a manner analogous to that given above. 34 g of the barium salt of the sulfoaldehyde (78%) was obtained from 13.5 g of the aldehyde.

10.347 mg substance: 5.060 mg $BaSO_4$. 7.570 mg substance: 3.560 mg $BaSO_4$. Found %: Ba 28.78, 28.80. $(C_5H_{10}O_4S)_2Ba \cdot H_2O$. Calculated %: Ba 28.29.

Sulfonation of heptaldehyde. 14 g of heptaldehyde was sulfonated by dioxanesulfotrioxide prepared from 10.5 g of sulfur trioxide in 60 ml of dichlorethane. After effecting the reaction and the usual processing, 20 g (65%) of the barium salt was obtained.

11.297 mg substance: 4.920 mg $BaSO_4$. 7.170 mg substance: 3.100 mg $BaSO_4$. Found %: Ba 25.63, 25.44. $(C_7H_{13}O_4S)_2Ba \cdot H_2O$. Calculated %: Ba 25.36.

6 g of the barium salt of sulfoheptaldehyde was oxidized in a manner analogous to that for sulfobutyraldehyde. The silver salt of valeric acid was obtained.

6.315 mg substance: 3.252 mg Ag. 6.289 mg substance: 3.254 mg Ag. Found %: Ag 51.50, 51.73. $C_5H_9O_2Ag$. Calculated %: Ag 51.62.

Sulfonation of octaldehyde. 12.5 g of octaldehyde was sulfonated in dichlorethane with dioxanesulfotrioxide prepared from 13.5 g of sulfur trioxide. 15.95 g (60%) of the barium salt was obtained.

8.290 mg substance: 3.580 mg $BaSO_4$. 7.455 mg substance: 3.195 mg $BaSO_4$. Found %: Ba 25.41, 25.22. $(C_8H_{15}O_4S)_2Ba$. Calculated %: Ba 24.89.

Sulfonation of decyl aldehyde. 15.5 g of decyl aldehyde was sulfonated with dioxanesulfotrioxide in dichlorethane, prepared from 8 g of sulfur trioxide. 13 g (43%) of the barium salt was obtained.

6.030 mg substance: 2.225 mg $BaSO_4$. 6.540 mg substance: 2.580 mg $BaSO_4$. Found %: Ba 23.42, 23.22. $(C_{10}H_{19}O_4S)_2Ba$. Calculated %: Ba 22.60.

15.5 g of decyl aldehyde was sulfonated in dichlorethane with dioxanesulfotrioxide prepared from 24 g of sulfur trioxide. 16 g (34%) of the barium salt of the disulfonic acid was obtained.

4.940 mg substance: 2.450 mg $BaSO_4$. 5.935 mg substance: 2.935 mg $BaSO_4$. Found %: Ba 29.11, 29.11. $C_{10}H_{18}O_7S_2Ba \cdot H_2O$. Calculated %: Ba 29.24.

Sulfonation of phenylacetaldehyde. 11 g of phenylacetaldehyde was sulfonated in dichlorethane with dioxanesulfotrioxide prepared from 8 g of sulfur trioxide. 19 g (57%) of the barium salt was obtained.

6.500 mg substance: 2.698 mg $BaSO_4$. 9.587 mg substance: 3.993 mg $BaSO_4$. Found %: Ba 24.42, 24.51. $(C_8H_7O_4S)_2Ba \cdot H_2O$. Calculated %: Ba 24.80.

5 g of the salt was oxidized by heating with an alkaline solution of potassium permanganate. The filtrate obtained was evaporated to a small volume and acidified with dilute hydrochloric acid. The crystals which formed were isolated and recrystallized from a small amount of water. A mixed melting point with benzoic acid gave no depression.

Sulfonation of acetone. 11.6 g of acetone was sulfonated by the slow addition of a solution of dioxanesulfotrioxide prepared from 18 g of sulfur trioxide. 21.8 g (53%) of the barium salt was obtained in the usual manner.

7.810 mg substance: 4.313 mg $BaSO_4$. 6.777 mg substance: 3.736 mg $BaSO_4$. Found %: Ba 32.50, 32.45. $(C_3H_5O_4S)_2Ba$. Calculated %: Ba 32.74.

7.9 g of acetone was sulfonated with dioxanesulfotrioxide prepared from 20 g of sulfur trioxide. 50 g of the barium salt was obtained.

7.370 mg substance: 4.540 mg $BaSO_4$. 5.240 mg substance: 3.230 mg $BaSO_4$. Found %: Ba 36.25, 36.27. $C_3H_4O_7S_2Ba \cdot H_2O$. Calculated %: Ba 36.86.

Sulfonation of dipropyl ketone. 19 g of the ketone was sulfonated with dioxanesulfotrioxide from 15 g of sulfur trioxide. 42 g (95%) of the barium salt was obtained.

7.757 mg substance: 3.490 mg $BaSO_4$. 7.967 mg substance: 3.590 mg $BaSO_4$. Found %: Ba 26.48, 26.52. $(C_7H_{13}O_4S)_2Ba$. Calculated %: Ba 26.14.

8.2 g of dipropyl ketone was sulfonated with dioxanesulfotrioxide from 13.4 g of sulfur trioxide. 40 g of the barium salt was obtained.

5.920 mg substance: 3.240 mg $BaSO_4$. 5.590 mg substance: 3.050 mg $BaSO_4$. Found %: Ba 32.21, 32.11. $C_7H_{12}O_7S_2Ba \cdot H_2O$. Calculated %: Ba 32.12.

Upon mixing solutions of disulfodipropyl ketone in the form of the barium salt and benzyl thiouronium chloride, an oil separated which crystallized rapidly on standing. M.p. 248° (from alcohol).

7.160 mg substance: 11.932 mg CO_2; 3.750 mg H_2O; 4.350 mg SO_4. 5.870 mg substance: 9.780 mg CO_2; 3.040 mg H_2O; 3.565 mg SO_4. Found %: C 45.48, 45.47; H 5.86, 5.80; S 20.27, 20.27. $C_{23}H_{34}O_7S_4N_4$. Calculated %: C 45.52; H 5.69; S 21.13.

5 g of the barium salt of sulfodipropyl ketone was oxidized by heating with a solution of chromic

anhydride in sulfuric acid. The mixture obtained was steam distilled. Propionic acid was separated in the form of the silver salt from the distillate.

8.345 mg substance: 4.983 mg Ag. Found %: Ag 59.71. $C_3H_5O_2Ag$. Calculated %: Ag 59.62.

Analogous results were obtained upon the oxidation of the barium salt of disulfodipropyl ketone.

Sulfonation of diisopropyl ketone. 34 g of the ketone was sulfonated in the usual manner with dioxanesulfotrioxide prepared from 25 g of sulfur trioxide. About 40 g (90%) of the barium salt was obtained.

6.720 mg substance: 3.033 mg $BaSO_4$. 7.247 mg substance: 3.260 mg $BaSO_4$. Found %: Ba 26.56, 26.47. $(C_7H_{13}O_4S)_2Ba$. Calculated %: Ba 26.14.

5 g of diisopropyl ketone was added to pyridinebisulfotrioxide prepared from 8 g of pyridinesulfotrioxide and 3.2 g of sulfur trioxide in 35 ml of dichlorethane. After 5 hours, it was processed in the usual manner. 12 g (80%) of the barium salt was obtained.

3.645 mg substance: 1.285 mg $BaSO_4$. 3.241 mg substance: 1.445 mg $BaSO_4$. Found %: Ba 26.12, 26.24. $(C_7H_{13}O_4S)_2Ba$. Calculated %: Ba 26.14.

8 g of sulfur trioxide in 25 ml of dichlorethane was added gradually with cooling and stirring to a solution of 11.4 g of diisopropyl ketone in 25 ml of dichlorethane. After 1 hour, the reaction mixture was processed in the usual manner. 19 g (72%) of the barium salt was obtained.

3.520 mg substance: 1.577 mg $BaSO_4$. Found %: Ba 26.37. $(C_7H_{13}O_4S)_2Ba$. Calculated %: Ba 26.14.

A solution of the barium salt of sulfodiisopropyl ketone formed a voluminous crystalline precipitate with benzyl thiouronium chloride. M.p. 142° (from alcohol).

7.160 mg substance: 12.860 mg CO_2; 4.350 mg H_2O. Found %: C 49.11; H 6.80. $C_{15}H_{24}O_4S_2N_2$. Calculated %: C 48.90; H 6.57.

Sulfonation of acetophenone. 18 g of acetophenone was sulfonated with dioxanesulfotrioxide from 14 g of sulfur trioxide. 40 g (90%) of the barium salt was obtained.

4.987 mg substance: 1.900 mg $BaSO_4$. 5.210 mg substance: 1.980 mg $BaSO_4$. Found %: Ba 22.42, 22.36. $(C_8H_7O_4S)_2Ba \cdot 4H_2O$. Calculated %: Ba 22.60. A crystalline salt with m.p. 152°, which corresponds to the literature data [3], was formed with benzyl thiouronium chloride.

8 g of the salt was oxidized with an alkaline solution of permanganate with heating. The benzoic acid obtained was identified by a mixed melting test with an authentic sample of bonzoic acid.

Sulfonation of cyclohexanone. 9.8 g of cyclohexanone was sulfonated with dioxanesulfotrioxide from 8 g of sulfur trioxide in an excess of dioxane. 21 g (85%) of the barium salt was obtained in the usual manner. A crystalline salt with m.p. 159-160° was obtained with benzyl thiouronium chloride, which corresponds to the literature data for cyclohexanone sulfonic acid [3].

SUMMARY

1. The action of various sulfonating agents, solution of sulfur trioxide in dichlorethane, pyridinesulfotrioxide, pyridine bisulfotrioxide, dioxanesulfotrioxide on various aldehydes and ketones of the aliphatic, alicyclic and arylaromatic series was studied.

2. It was shown that the most convenient sulfonating agent for aldehydes was dioxanesulfotrioxide, while all of the above agents, with the exception of pyridinesulfotrioxide, could be used for ketones.

3. The sulfonic acids, obtained in the form of the barium salts, of propionaldehyde, butyraldehyde, isobutyraldehyde, isovaleraldehyde, octaldehyde, and decyl aldehyde were obtained for the first time.

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* See Consultants Bureau translation, p. 189.

STERIC HINDRANCE IN ORGANO-MAGNESIUM REACTIONS

XV. SYNTHESIS OF ALKOXY-CONTAINING SECONDARY α-HYDROXY ACID ESTERS

I. I. Lapkin

In the previous communications [1-4], a method for the preparation of esters of secondary α-hydroxy acids based upon the reaction of organo-magnesium compounds with oxalic ester was reported. In order to extend the application of this method, the present investigation was conducted to ascertain the possibilities of synthesizing alkoxy-containing α-hydroxy acid esters with this method. The results obtained are given in the Table.

These results show that the reaction proceeds normally, and that the cleavage of the alkoxy group by the action of the organo-magnesium compound does not occur.

EXPERIMENTAL

(Together with L. L. Grachev, G. N. Kozlov, N. S. Budrina, V. P. Potavov, and A. T. Boyarshina).

1. Reaction of β-methoxy-α-naphthyl magnesium bromide with diethyl oxalate (ratio 1:1). Since β-methoxy-α-naphthyl magnesium bromide was poorly soluble in absolute ether, the preparation of the organo-magnesium compound was effected in an ether-toluene (1:1) solvent. 33.8 g (1/7 mole) of α-bromo-β-methoxy-naphthalene, 4.5 g of magnesium, and 21.0 g (1/7 mole) of diethyl oxalate were used to conduct the experiment.

The prepared solution of β-methoxy-α-naphthyl magnesium bromide was added, with cooling and mechanical stirring, to an ether solution of diethyl oxalate. The reaction mixture was heated for 6 hours and decomposed with water and 10% acetic acid. The ether toluene layer was separated from the aqueous. Upon standing, a white residue of magnesium oxalate ($MgC_2O_4 \cdot H_2O$) separated in 4.3 g quantity.

The ether-toluene layer was washed with a 10% sodium carbonate solution, with water to a neutral reaction, and dried with anhydrous sodium sulfate. After removal of the solvent, the mixture of substances obtained was subjected to fractional vacuum distillation at 9 mm: Fraction I, to 185°, Fraction II, 185-235°, 18.8 g ; residue in flask, 3 g. 15.2 g (41%) of ethyl 2-methoxynaphthyl-1-glycolate was isolated by the redistillation of Fraction II. B.p. 183-185° at 5 mm; m.p. 92° (from a mixture of petroleum ether and toluene).

0.1082 g substance: 0.2737 g CO_2; 0.0598 g H_2O. 0.0526 g substance: 4.4 ml CH_4 (18°, 760 mm).
Found %: C 69.03; H 6.18; OH 6.3. $C_{15}H_{16}O_4$. Calculated %: C 69.21; H 6.20; OH 6.5.

The ester obtained was not reported in the literature.

The ester was saponified by heating with a 5% alcohol alkali solution. The 2-methoxynaphthyl-1-glycolic acid had an m.p. 126-127° (from aqueous methyl alcohol).

0.1121 g substance: 0.2753 g CO_2; 0.0519 g H_2O. 0.1028 g substance: 4 ml 0.1 N $AgNO_3$.
Found %: C 67.03; H 5.18; OCH_3 12.1. $C_{13}H_{12}O_4$. Calculated %: C 67.23; H 5.21; OCH_3 13.4.

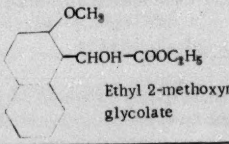
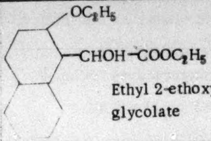
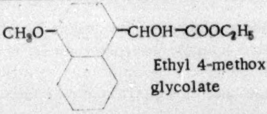
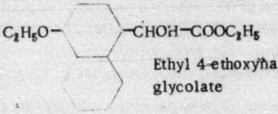
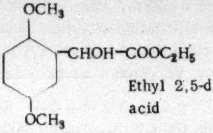
2. Reaction of β-ethoxy-α-naphthyl magnesium bromide with diethyl oxalate (ratio 1:1). 36 g (1/7 mole) of 1-bromo-2-ethoxynaphthylene, 4.5 g of magnesium, and 21 g (1/7 mole) of diethyl oxalate were used for the reaction.

The reaction conditions were the same as for the previous experiment. The mixture of products obtained was vacuum distilled at 6 mm: Fraction I, to 170°; Fraction II, 170-230°, 19.0 g; residue 2 g. 15.2 g (40%) of ethyl 2-ethoxynaphthyl-1-glycolate was isolated upon the redistillation of the second fraction. B.p. 186-188° at 4 mm; m.p. 62° (from a mixture of petroleum ether and toluene).

0.1091 g substance: 0.2797 g CO_2; 0.0633 g H_2O. 0.1082 g substance: 9.3 ml CH_4 (17°, 759 mm).
Found %: C 69.95; H 6.51; OH 6.1. $C_{16}H_{18}O_4$. Calculated %: C 70.05; H 6.61; OH 6.2.

2-Ethoxynaphthyl-1-glycolic acid was obtained by the saponification of the ester; m.p. 137-138° (from toluene).

0.1033 g substance: 0.2574 g CO_2: 0.0521 g H_2O. Found %: C 68.00; H 5.64. $C_{14}H_{14}O_4$. Calculated %: C 68.28; H 5.73.

Expt. No.	Reaction Components	Ratio of Components	Formula of substance	Yield of substance
1	β-Methoxy-α-naphthyl-magnesium bromide + diethyl oxalate	1:1	 Ethyl 2-methoxynaphthyl-1 glycolate	41
2	β-Ethoxy-α-naphthyl magnesium bromide + diethyl oxalate	1:1	 Ethyl 2-ethoxynaphthyl-1-glycolate	40
3	4-Methoxy-1-naphthyl magnesium bromide + diethyl oxalate	1:1	 Ethyl 4-methoxynaphthyl-1-glycolate	45
4	4-Ethoxy-1-naphthyl magnesium bromide + diethyl oxalate	1:1	 Ethyl 4-ethoxynaphthyl-1-glycolate	42
5	2,5-Dimethoxyphenyl magnesium bromide + diethyl oxalate	1:1	 Ethyl 2,5-dimethoxymandelic acid	40

2-Ethoxynaphthyl-1-glycolic acid and ethyl ester had not been reported in the literature.

3. Reaction of 4-methoxy-1-naphthyl magnesium bromide with diethyl oxalate (ratio 1:1). An ether-toluene solution of 4-methoxy-1-naphthyl magnesium bromide, prepared from 47.4 g (0.2 mole) of 1-bromo-4-methoxynaphthylene, and 6 g of magnesium, was added with cooling and mechanical stirring to an ether solution of 29.2 g (0.2 mole) of diethyl oxalate. The mixture was heated for 6 hours, and then, as usual, the magnesium complex was decomposed by water and 10% acetic acid. 4.4 g of greenish yellow crystals separated on standing from the dried ether layer. After separation of these crystals and removal of the solvents, the mixture of substances was vacuum distilled. 23 g (45%) of ethyl-4-methoxynaphthyl-1-glycolate was obtained. B.p. 200-202° at 8 mm, m.p. 84° (from a mixture of petroleum ether and toluene).

0.0794 g substance: 0.2010 g CO_2: 0.0440 g H_2O. 0.0697 g substance: 6.3 ml CH_4 (22°, 758 mm). Found %: C 69.09; H 6.21; OH 6.3. $C_{15}H_{16}O_4$. Calculated %: C 69.21; H 6.20; OH 6.5.

The greenish-yellow crystals isolated above from the ether solution were heated with toluene, resulting in part of them going into solution. This part of the crystals was purified by recrystallization from that solvent. The yellow crystals of 4,4'-dimethoxy-1,1'-naphthyl had a m.p. 229-230°. According to literature data [5], 4,4'-dimethoxy-1,1'-naphthyl has a m.p. 228-229°.

0.1001 g substance: 0.2844 g CO_2; 0.0440 g H_2O. 0.1330 g substance: 7.1 ml 0.1 N $AgNO_3$. Found %: C 77.53; H 4.91; OCH_3 16.54. $C_{24}H_{18}O_4$. Calculated %: C 77.82; H 4.90; OCH_3 16.75.

That part of the crystals which was insoluble in toluene was purified by recrystallization from acetone.

The colorless crystals of 4,4'-dimethoxy-1,1'-naphthoin had an m.p. 238°.

0.1062 g substance: 0.3004 g CO_2; 0.0508 g H_2O. 0.1260 g substance: 6.7 ml 0.1 N $AgNO_3$. 0.0664 g substance: 4.2 ml CH_4 (18°, 758 mm). Found %: C 77.19; H 5.35; OCH_3 16.5; OH 4.5. $C_{24}H_{20}O_4$. Calculated %: C 77.40; H 5.41; OCH_3 16.6; OH 4.6.

4,4'-Dimethoxy-1,1'-naphthoin has not been reported in the literature.

4. Reaction of 4-ethoxy-1-naphthyl magnesium bromide with diethyl oxalate (ratio 1:1). Starting substances 36 g (1/7 mole) of 1-bromo-4-ethoxynaphthylene, 4.5 g magnesium, and 21 g (1/7 mole) of a diethyl oxalate.

The reaction conditions were the same as in the first experiment. 16.4 g (42 %) of ethyl 4-ethoxynaphthyl-1-glycolate was obtained. B.p. 192-194° at 5 mm; m.p. 76-77° (from a mixture of petroleum ether and toluene).

0.1247 g substance: 0.3200 g CO_2; 0.0710 g H_2O. 0.1070 g substance: 9.2 ml CH_4 (18°, 758 mm). (according to Terentyev). Found %: C 70.04; H 6.37; OH 6.1. $C_{16}H_{18}O_4$. Calculated %: C 70.05; H 6.61; OH 6.2

This ester was saponified by a 5% alcoholic alkali solution. Colorless crystals of 4-ethoxynaphthyl-1-glycolic acid, having an m.p. 127°, was obtained.

0.1174 g substance: 0.2931 g CO_2; 0.0583 g H_2O. 0.0557 g substance: 10.7 ml CH_4 (18°, 758 mm). 0.1030 g substance: 0.0957 g AgI. Found %: C 68.15; H 5.59; OH 13.6; OC_2H_5 17.4. $C_{14}H_{14}O_4$. Calculated %: C 68.28; H 5.73; OH 13.8; OC_2H_5 18.3.

There is no report in the literature of 4-ethoxy-1-glycolic acid or its ethyl ester.

The product of the second stage of the reaction was not obtained.

5. Reaction of 2,5-dimethoxyphenyl magnesium bromide with diethyl oxalate (ratio 1:1). 36.2 g (1/6 mole) of 1-bromo-2,5-dimethoxybenzene, 5 g of magnesium, and 24.4 g (1/6 mole) of diethyl oxalate were used. The reaction conditions were the same as in the first experiment.

16 g (40%) of ethyl 2,5-dimethoxymandelate was obtained. B.p. 168-170° at 6 mm.

d_4^{20} 1.2241; n_D^{20} 1.5322; MR_D 60.77; calculated 60.24.

0.1098 g substance: 0.2440 g CO_2; 0.0654 g H_2O. 0.0932 g substance: 9.2 ml CH_4 (20°, 761 mm) (according to Terentyev). Found %: C 59.81; H 6.68; OH 6.9. $C_{12}H_{16}O_2$. Calculated %: C 60.60; H 6.71; OH 7.1.

2,5-Dimethoxymandelic acid with m.p. 97-98° (from methyl alcohol) was obtained by the saponification of the ester. An m.p. 98-103° is given in the literature [6] for this acid.

0.1279 g substance: 0.2644 g CO_2; 0.0646 g H_2O. 0.0706 g substance: 16.0 ml CH_4 (20°, 758 mm). 0.0913 g substance: 8.0 ml 0.1 N $AgNO_3$. Found %: C 56.41; H 5.65; OH 15.7; OCH_3 27.2. $C_{10}H_{12}O_5$. Calculated %: C 56.60; H 5.70; OH 16.0; OCH_3 29.2.

SUMMARY

The study of methods for the preparation of esters of secondary α-hydroxy acids based on the reaction of organomagnesium compounds and oxalic acid esters was continued. It was shown that esters of alkoxy-containing α-hydroxy acids could be synthesized by this method.

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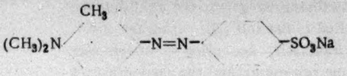
COPLANARITY OF THE DIMETHYLAMINO GROUP WITH THE BENZENE RING AND ITS AUXOCHROMIC ACTION. II.

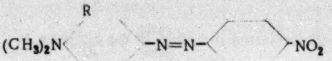
A. I. Kiprianov and I. N. Zhmurova

The subject of the previous communication [1] was the effect of steric hindrance on the auxochromic action of the dimethylamino group in aminothiocarbocyanines. In the present investigation, the same problem was studied in relation to certain azo dyes. For this purpose, the simplest amino azo dyes containing alkyl radicals in the ortho position to the dimethylamino group were synthesized and investigated optically. Certain preparations of this type were previously known. Hantzsch observed that the methyl homolog of methyl orange is practically lacking in indicator properties. Upon acidification, the color of the solution fades, and the absorption curve becomes similar to that of azobenzene [2]. Similar properties were found by Hantzsch for the o-methyl derivative of p-dimethylaminobenzene [3]. Later, it was found that the introduction of the methyl in vicinity to a dimethylamino group in the 4-dimethylamino-4'-nitroazobenzene molecule shifts the absorption maximum by 40 $m\mu$ toward the lower wave lengths [4]. Recently, results were published on the effect of five and six-membered rings condensed with the benzene nucleus in the vicinity of a dimethyl amino group on the color of amino azo dyes [5].



It seemed desirable to show how the color of the azo dye changes if a radical of increasing size is introduced into the ortho position to the dimethylamino. For this purpose, 4 azo dyes of the structure (a) were prepared where R = H, CH_3, C_2H_5, and iso-C_3H_7.

The absorption maxima and the molecular extinctions of these preparations, in neutral and acidic alcoholic solutions, are given in Table 1, and the corresponding absorption curves, in Fig. 1.



(a)

In acidic solutions, the measurement was effected in a mixture of 1 volume of conc. hydrochloric acid and 3 volumes of alcohol.

In neutral alcoholic solution, the substitution of a hydrogen atom, in the ortho position to the dimethylamino group by a methyl, causes a shift in the absorption maximum of the preparation by 37 $m\mu$ toward the lower wavelengths (according to Blumberg [4] by 40 $m\mu$). The transition from the methyl group to the ethyl group of greater volume, increases the shift of the maximum to 50 $m\mu$, the isopropyl reacts still more strongly (55 $m\mu$). The intensity of absorption decreases with the increase in the volume of the substituent. Therefore, the ortho substituent partially cuts off the effect of the dimethyl amino group on the color of the amino azo dyes, as well as on amino cyanines, shifting it from the plane of the benzene ring.

TABLE 1

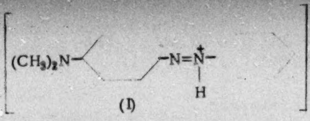
Dye No.	R	In alcohol		In alcohol + HCl	
		λ_{max}, $m\mu$	$\epsilon \cdot 10^{-4}$	λ_{max} $m\mu$	$\epsilon \cdot 10^{-4}$
1	H.	475	3.2	508	5.68
2	CH_3	438	2.2	508	0.26
3	C_2H_5. . . .	425	2.18	490	0.10
4	iso-C_3H_7. .	420	1.86	460	0.06

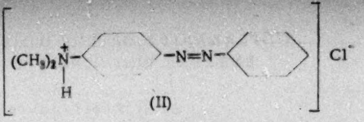
In acidic solution, the absorption maximum of dye 1 (R = H) undergoes a strong shift toward the longer wavelengths, from 475-508 $m\mu$; the intensity of the absorption increases. This occurrence, usual for many amino azo dyes, is due to the formation of salts with the azo group (I).

With dyes 2,3, and 4 in acidic solution, however, a strong decrease in the intensity of absorption was found. These dyes, as the methyl homologs of methyl orange, are faded to a considerable extent by acidity.

On the basis of Hantzsch's investigations [6], it is known that the different reaction of the amino azo dyes to acids is due to the fact that they can form salts, not only of the azo group, (I), but also of type (II) on the amino groups which are tautomeric with them, (see top of next page).

The latter results in the complete exclusion of the auxochrome. The absorption of salts of type (II) is identical to that of the corresponding derivatives of azobenzene. According to Hantzsch, solutions of amino azo compound salts are equilibrium mixtures of tautomers (I) and (II). In most of the dyes, the equilibrium is shifted toward the salt


(I)


(II)

(I), called the quinoid by Hantzsch. These dyes give an intense red violet colored solution upon acidification. But for certain dyes, among them being those containing substituents in the ortho position to the dimethylamino group, the equilibrium is shifted to the salt (II), called the azoid by Hantzsch. According to modern electronic representation, the predominance of salts of type (I) or (II) must depend on the electron density on the nitrogen atom in the azo group. In the amino derivatives of azobenzene, this density is higher than in azo benzene itself because of the electron donor character of the amino. Upon the destruction of the coplanarity of the dimethylamino group and the benzene ring, the electron pair on the nitrogen atom loses the possibility to locate on the benzene ring, and subsequently on the azo group. As a result, the electron density on the nitrogen atom of the azo group decreases, that on the amino group increases, and salt formation is shifted in the direction of the amino group.

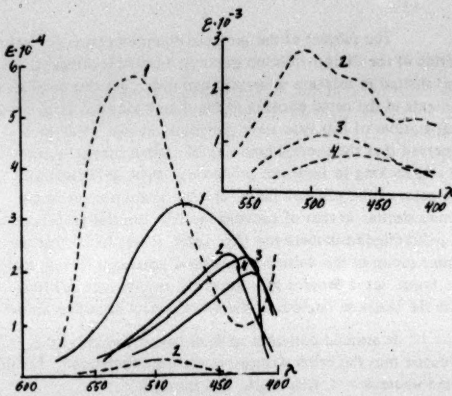
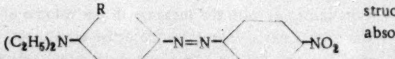


Fig. 1. Continuous curves, solvent alcohol; broken, solvent alcohol + HCl.

In acidic solutions of preparations 2 and 3, a small amount of the salt molecules are still found in the quinoid form (the absorption maxima are 508 mμ and 490 mμ respectively). In preparation 4, where, in addition to the dimethylamino group, there is a large isopropyl group, the equilibrium is almost completely shifted in the direction of the azoid salt. The absorption maxima and the molecular extinction of the solution of this salt accurately coincide with those of p-nitroazobenzene.

The same effect as the increase of the volume of the ortho substituent is given by the increase in the volume of the alkyls on the amino group. This is apparent from a comparison of the absorption of two azo dyes of structure (b) which were investigated, where R = H or CH_3. Their absorption maxima and extinctions are given in Table 2.

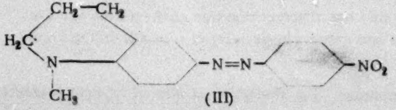

(b)

Changing the dimethylamino group by a diethylamino group, increases the shift of the maximum upon the introduction of an ortho methyl from 37mμ to 70 mμ.

TABLE 2

Dye No.	R	In alcohol		In alcohol + HCl	
		λ_{max}, mμ	$\epsilon \cdot 10^{-4}$	λ_{max}, mμ	$\epsilon \cdot 10^{-4}$
5	H	490	3.70	510	3.11
6	CH_3	420	2.13	460-480	0.07

If the dialkyl amino group and the ortho substituent are closed into a nitrogen heterocycle, it is stably fixed in the plane of the benzene ring, in this case, there is only the normal quinoid salt. The dye (III), which was synthesized by the authors, has an absorption maximum of 496 mμ in alcohol with a molecular extinction of $3.6 \cdot 10^{-4}$. In acidic solution, its absorption maximum is 512 mμ, and its extinction $6.66 \cdot 10^{-4}$.


(III)

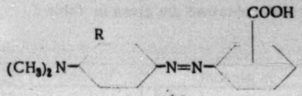
The effect of steric hindrance on the properties of the indicator dyes is of great interest. Table 3 gives the absorption maxima and extinction of methyl orange and its methyl homolog in weakly basic and acidic solutions (the older data of Hantzsch is more qualitative in character).

TABLE 3

Dye No.	R	Basic solution		Acidic solution	
		λ_{max}, mμ	$\epsilon \cdot 10^{-4}$	λ_{max}, mμ	$\epsilon \cdot 10^{-4}$
7	H	460	2.46	505	4.43
8	CH_3	425	1.15	495	0.06

The methyl homolog of methyl orange, similarly to other amino azo dyes with steric hindrances, forms predominantly the azoid salt in acidic solution and is inapplicable as an indicator.

Methyl red and both its isomers, meta- and para-derivatives, as well as their methyl homologs (c) were investigated, where R=H CH_3.



(c)

As is known, only one isomer possesses indicator properties, the one with the carboxyl in the ortho position to the azo group. With the meta- and para- isomers, the transition of the color occurs gradually and is completed only by the addition of a large excess of acid. The methyl homologs of these dyes were unknown up to now.

Table 4 gives the optical data for methyl orange and its derivatives.

TABLE 4

Dye No.	R	Position of COOH	Basic solution		Acidic solution	
			λ_{max}, mμ	$\epsilon \cdot 10^{-4}$	λ_{max}, mμ	$\epsilon \cdot 10^{-4}$
9	H	ortho	435	1.90	520	4.54
10	CH_3	ortho	430	1.72	505	4.50
11	H	meta	435	2.35	513	4.10
12	CH_3	meta	425	1.05	513	0.77
13	H	para	455	2.65	515	6.00
14	CH_3	para	422	1.53	507	0.31*

Fig. 2 shows the absorption curve for the dyes listed in Table 4 in acidic and basic solutions.

It could be expected that the methyl homolog of methyl red would be colorless in acidic medium like the methyl homolog of methyl orange. Unexpectedly, it was found however, that the introduction of a methyl radical into the ortho position to the dimethylamino group did not essentially change the properties of methyl red. The absorption maxima of the two dyes in basic and acidic solutions differ only 5 mμ, and the extinction is almost identical. The methyl homolog of methyl red can be successfully applied as an indicator. The transition of the color of methyl red occurs at a pH of 4.4 - 6.2. For the methyl homolog, it is 4.66 - 6.56 (the transition interval was measured by the buffer method at the transition points, the pH value was controlled by a pH meter). The introduction of a methyl into the meta and para isomer has the usual effect. These dyes are colorless in acidic solutions, forming the azoid salt predominantly.

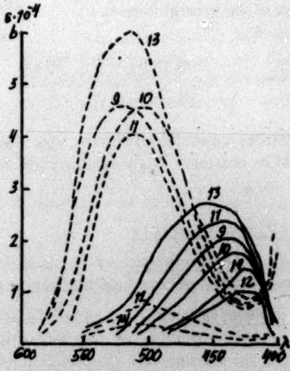
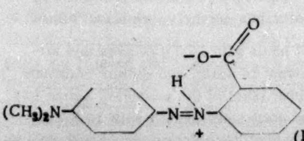


Fig. 2. Continuous curves, basic solution, broken, acidic solution.

The unusual behavior of the methyl homolog of methyl red must, evidently, be due to the unusualness of methyl red itself. Methyl red differs from its isomers in that it alone is an indicator, i.e., completely forms salts in a narrow pH interval. It appears that the unusualness of the chemical nature of methyl red and its methyl homolog is due to the fact that the formation of a hydrogen bond between the nitrogen atom of an azo group and the carbonyl (IV), as a result of the addition of a proton to the yellow dye anion, is possible in the molecules of these compounds:



(IV)

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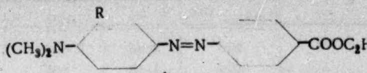
* Dye 14 could not be completely purified.

The possibility of the formation of such a hydrogen bond forces the molecule of the methyl homolog of methyl red to add a proton, not on the amino group, but on the azo group. The idea of the ring structure of salts of methyl red was put forth by Thiel [7], back in 1923.

Ethyl esters of structure (g), where R = H, CH_3, were studied, in addition to the derivatives of methyl red.



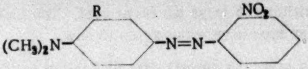
(d)

The results obtained are given in Table 5.

TABLE 5

Dye No.	R	In alcohol		In alcohol + HCl	
		λ_{max}, mμ	$\epsilon \cdot 10^{-4}$	λ_{max}, mμ	$\epsilon \cdot 10^{-4}$
15	H	460	2.85	510	3.75
16	CH_3	425	1.55	440–460	0.06

The formation of a hydrogen bond can also be postulated in salts of nitro derivatives of p-dimethylaminoazobenzene (e). For this reason preparations of this type were made, and their spectra studied in neutral and acidic alcoholic solutions. However, as it is apparent from Table 6, the effect of the methyl in this case is very strong. Preparation 18 is decolorized by acids, i.e., it forms a salt on the amino group. Apparently, salts on the azo group cannot be formed because of the attraction of the electrons by the nitro group. This even occurred with the unsubstituted dye 17. Its molecular extinction is smaller in acidic medium than in neutral, whereas the opposite usually occurs.

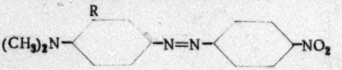


(e)

TABLE 6

Dye No.	R	In alcohol		In alcohol + HCl	
		λ_{max}, mμ	$\epsilon \cdot 10^{-4}$	λ_{max}, mμ	$\epsilon \cdot 10^{-4}$
17	H	440	2.68	500	1.11
18	CH_3	425	1.01	440–460	0.04

With the dialkylanilines which have substituents ortho to the dialkylamino group capable of electrophilic reactions, substitution is greatly decreased. For this reason, these compounds couple with much greater difficulty with diazonium compounds than amines which are unsubstituted in the ortho position. With the active diazonium compounds, p-nitrophenyl diazonium, p-sulfophenyl diazonium, and diazotized amino benzoic acids, dimethyl o-toluidine couples satisfactorily. But upon increasing the volume of the radical in the ortho position, the yield of the coupling products is greatly diminished, and the purification is very difficult because of the incapability of the products to crystallize. Table 7 shows the effect of the volume of radical R on the yield of the dye of the general formula (f):



(f)

TABLE 7

R	Yield of the dye in % of theoretical
H	71
CH_3	57
C_2H_5	33
iso-C_3H_7	9

Dimethyl-o-toluidine and its derivatives almost completely do not couple with diazonium compounds which contain electro positive substituents, as for example p-anisidine and p-phenetidine. In these cases not even traces of the dyes could be obtained. Dialkylanilines with two ortho substituents do not couple with any diazonium compounds [8].

EXPERIMENTAL

Intermediate Products

Dimethyl-o-toluidine was obtained by a method reported in one of the patents [9] by the condensation of o-toluidine with chloroacetic acid followed by the decarboxylation of the N,N-dicarboxymethyl-o-toluidine formed.

o-Isopropyldimethylaniline. 12.7 g of o-anisidine [10] was heated for 4 hours with 10.5 g of dimethyl sulfate at 130-140°. The glass-like mass formed was dissolved in the minimum amount of water, and sodium carbonate was added to the solution until the evolution of carbon dioxide stopped. The upper layer of the secondary amine was separated, dried with a small amount of fused potassium carbonate, filtered, and once more treated with 10.5 g of dimethyl sulfate under the same conditions. The product was separated, as in the first methylation, dried with potassium carbonate, and distilled. The tertiary amine obtained in this manner, did not even contain traces of the secondary amine. Yield 8.5 g or 62%*. B.p. 202-202.5°**.

Found %: N 8.47, 8.65. $C_{11}H_{17}N$. Calculated %: N 8.58.

o-Ethyldimethylaniline was prepared by the methylation of o-ethylaniline [11] in a manner analogous to the previous preparation. B.p. 196-199°, which corresponded to the literature data [12].

Diethyl-o-toluidine was prepared by the ethylation of o-toluidine with diethyl sulfate in two stages in a manner analogous to the previous compound. B.p. 207-209°, which corresponded to the literature data [13].

Dyes

4-Diethylamino-4'-nitroazobenzene [14], 1, and 4-diethylamino-4-nitroazobenzene [15], 5 were prepared by the coupling of p-nitrophenyldiazonium with dimethylaniline and diethylaniline.

3-Methyl-4-dimethylamino-4'-nitroazobenzene [16], 2, and 3-methyl-4-diethylamino-4'-nitroazobenzene [15], 6 were prepared by the coupling of p-nitrophenyldiazonium with dimethyl-o-toluidine and diethyl-o-toluidine in aqueous alcoholic solution in the presence of sodium acetate.

3-Ethyl-4-dimethylamino-4'-nitroazobenzene 3. 0.5 g of p-nitroaniline was diazotized and added to a mixture of o-ethyldimethylaniline, 5 ml of alcohol, and 2.5 g of crystalline sodium acetate, which was cooled with ice. The precipitated dye was filtered and recrystallized from alcohol. Orange scales: m.p. 85-87°. Yield 0.3 or 33%.

Found %: N 18.66, 18.61. $C_{16}H_{18}O_2N_4$. Calculated %: N 18.71.

3-Isopropyl-4-dimethylamino-4'-nitroazobenzene, 4, was prepared in a manner analogous to the previous preparation from 0.5 g of p-nitroaniline and 0.5 g of o-isopropyldimethylaniline. The dye precipitated in the form of an oil. The oil was extracted with chloroform, the chloroform was evaporated, the residue was dissolved in a small amount of H_2SO_4 (1:1). The oil crystallized, the crystals were pressed on a porous plate, and recrystallized from alcohol. During this recrystallization several drops of ammonia were added to the alcohol. Orange scales. Yield 0.1 g or 9%; m.p. 102-104°.

Found %: N 17.80, 17.73. $C_{17}H_{20}O_2N_4$. Calculated %: N 17.95.

1-Methyl-6-(4'-nitrophenylazo)-tetrahydroquinoline. 1.7 g of p-nitroaniline was diazotized and added to a cooled solution of 1.7 g of N-methyltetrahydroquinoline [17] in 10 ml of 10% HCl. After several minutes, the dye precipitated and was filtered, washed with water, and dried in a desiccator. The yield of the crude dye was 3 g or 88%. For purification, the dye was chromatographed from a benzene solution on aluminum oxide, and then recrystallized from ligroin. M.p. 159-160°.

Found %: N 18.60, 18.18. $C_{18}H_{16}O_2N_4$. Calculated %: N 18.91.

3-Methyl-4-dimethylamino-4'-sulfoazobenzene 8. 2 g of sulfanilic acid was mixed with 10 ml of water, and 1.2 g of dimethyl-o-toluidine was added. The mixture was cooled to 0°, and 0.8 g of $NaNO_2$ in 10 ml of water was added with efficient stirring. The sodium salt of the dye was salted out with NaCl, filtered, and dissolved in 3 ml of 60% acetic acid. The dye dissolved initially, and then the free sulfonic acid precipitated. Fine, yellow platelets (from water). Yield 0.5 g or 18%.

Found %: N 12.91, 12.78. $C_{15}H_{17}O_3N_3S$. Calculated %: N 13.15.

The dye was first prepared by Hantzsch; however, the detailed method of preparation was not given by him [2].

3-Methyl-4-dimethylamino-2'-carboxyazobenzene, 10. 8 g of anthranilic acid was dissolved in 20 ml of 8% NaOH, and a solution of 4 g of $NaNO_2$ in 50 ml of water was added. The mixture was cooled to 0° and added to 25 ml of cold 8% HCl. The diazo solution was stirred for 10 minutes and added to a cold solution of 6 g of dimethyl-o-toluidine in 50 ml of 4% HCl. The mixture was left to stand over night in the cold. The precipitated mass was filtered and extracted with boiling toluene. 2 g (14%) of an amorphous dye was obtained. After several recrystallizations from toluene, a microcrystalline powder was obtained. M.p. 185-187°.

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* The yield here and below is given in per cent of the theoretical.

** The boiling and melting points here and elsewhere are corrected.

Found %: N 14.73, 15.02. $C_{16}H_{17}O_2N_3$. Calculated %: N 14.84.

4-Dimethylamino-3'-carboxyazobenzene, 11. 0.5 g of m-aminobenzoic acid was diazotized and added to a solution of 0.5 g of dimethylaniline in 25 ml of 8% HCl. After several minutes, 1 g of crystalline sodium acetate was added. The precipitated dye was filtered and recrystallized from toluene. Orange needles. Yield 0.68 g or 68%. M.p. 207-208°. Thiel[18] gives an m.p. 210° for the preparation.

3-Methyl-4-dimethylamino-3'-carboxyazobenzene, 12, was prepared analogously to the previous preparation by the coupling of the diazotized m-aminobenzoic acid with dimethyl-o-toluidine. The yield of the crude product was 47.5%. Orange needles (from ligroin); m.p. 159-161°.

Found %: N 14.34, 14.44. $C_{16}H_{17}O_2N_3$. Calculated %: N 14.84.

4-Dimethylamino-4'-carboxyazobenzene, 13, was first prepared by Hantzsch [19] in the form of the Na salt and hydrochloride. The free acid was not characterized by him, or by other investigators [18, 20]. This dye was prepared analogously to dye 11. 0.75 g or 75% of the crude dye was obtained from 0.5 g of p-aminobenzoic acid and 0.5 g of dimethylaniline. Fine red needles (from alcohol); m.p. 251-252° with decomp.

Found %: N 15.42, 15.56. $C_{15}H_{15}O_2N_3$. Calculated %: N 15.67.

3-Methyl-4-dimethylamino-4'-carboxyazobenzene, 14, was prepared in a 50% yield in the form of an amorphous powder analogously to the previous preparation. The dye could not be isolated in the pure state because of its poor solubility in most organic solvents.

4-Dimethylamino-4'-carboethoxyazobenzene, 15. 0.25 g of ethyl p-aminobenzoate was diazotized and added to a solution of 0.2 g of dimethylaniline in 5 ml of 10% HCl. 1 g of sodium acetate was added. The dye was filtered and recrystallized from alcohol. Orange tablets; m.p. 158-160°. Hantzsch [3] gives an m.p. 160° for this preparation.

3-Methyl-4-dimethylamino-4'-carbethoxyazobenzene, 16, was obtained analogously to the previous preparation from 0.25 g of ethyl p-aminobenzoate and 0.2 g of dimethyl-o-toluidine. The dye precipitated first as an oil which crystallized later. The yield after recrystallization was 0.18 g or 20%. Orange needles (from alcohol); m.p. 76-78°.

Found %: N 13.90, 13.75. $C_{18}H_{21}O_2N_3$. Calculated %: N 13.51.

4-Dimethylamino-2'-nitroazobenzene, 17, was prepared by the coupling of o-nitrophenyldiazonium with dimethylaniline. M.p. 127°, which corresponds to the literature data [21].

3-Methyl-4-dimethylamino-2'-nitroazobenzene, 18. 1.4 g of o-nitroaniline was diazotized and added to a mixture of 1.2 g of dimethyl-o-toluidine, 6 ml of 10% HCl, and 8 g of crystalline sodium acetate. The dye precipitated in the form of an oil. The oil was separated from the water by decantation and dissolved in a small amount of concentrated H_2SO_4. The solidified mass was pressed on a porous plate and recrystallized from alcohol. The preparation obtained in this manner was the dye sulfate. The yield was 0.33 g or 10%. Orange rhomboids, M.p. 191-193°, with decomp. An oil which could not be crystallized was obtained on treatment of the salt with ammonia.

Found %: N 14.80, 14.73; S 8.60, 8.67. $C_{15}H_{13}O_2N_4 \cdot H_2SO_4$. Calculated %: N 14.81; S 8.49.

SUMMARY

1. In order to study the effect of steric hindrance on the auxochromic action of the dialkylamino group in the azo dye, seventeen azo dyes, 8 of them new, were synthesized and investigated.

2. It was shown that the introduction of a substituent in the ortho position to the dialkylamino group partly removes its auxochromic effect, as shown by shift in the absorption maximum of the dye toward the shorter wavelengths, and a decrease in the intensity of absorption.

3. It was shown that azo dyes containing substituents in the ortho position to the dialkylamino group decolorized in acidic medium: the intensity of their color decreases ten-fold and resembles that of azobenzene. With the absence of an ortho substituent the color of the dye solution is deepened by acidification, and the intensity increased. This phenomenon is explained by the fact that dyes containing substituents in the ortho position to the dialkylamino group form salts on the dialkylamino group, not on the azo group. The formation of such salts on the

dialkylamino group completely removes its auxochromic action. The methyl homolog of methyl red is an exception, which, in spite of the presence of steric hindrance, forms salt on the azo group.

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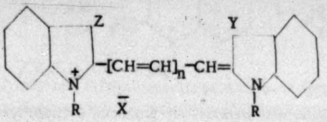
INVESTIGATIONS OF CYANINE DYES

I. QUINO-, QUINOID-, AND QUINOTHIACARBOCYANINES

G. T. Pilyugin and Z. Ya. Krainer

Questions on the theory of color and the establishment of the relationship between the color of molecules and their structure historically were solved chiefly by the investigations on dyes of the triphenylmethane series. However, within the last 20 years, polymethine dyes of the cyanines type have acquired great importance in investigations on color problems.



The characteristic property of their structure is the relative simplicity and the ability conveniently to change the composition of part of the molecule, which is convenient for the study of the relation of color of the molecule and its structure. In addition, molecules of these dyes give absorption spectra with sharply defined maxima, which is not found in other classes of dyes. This optical property is of essential value for the study of problems on the theory of color.

The effect of substitution on the various positions of the benzene ring of the heterocyclic base on the color of the cyanine dye is of scientific interest. The effect of polar substituents on the color of thiacarbocyanine molecules was extensively investigated by Kiprianov, Ushenko, and Sych [1] who studied the effect of electropositive substituents, introduced symmetrically into the 6,6' position and showed that all of these compounds shift the absorption maximum, as compared to the unsubstituted, toward the higher wave lengths, and are arranged by their bathochromic effect in a series corresponding to the order to activity as:

$$H < Cl < OCH_3 < CH_3 < I < OC_2H_5 < OH < SH < NHSO_2C_6H_4CH_3 < NHCOCH_3 < NH_2 < S < NHCH_3 < NHC_2H_5 < N(CH_3)_2.$$

Kiprianov and Ushenko also investigated [2] the action of electronegative substituents introduced into the 6,6' positions of the thiacarbocyanines on the color. It was mentioned that these substituents also deepened the color. The greatest shift in the absorption maximum was caused by the nitro group, then followed the carboxy, sulfo, and their derivatives.

The effect of the position of the substituent in the benzene ring of the heterocycle base on the color was mainly studied by Levkoev, Sveshnikov, and Kheifits [3] on the symmetrically disubstituted dimethoxycarbocyanines. It was mentioned by them that thiacyanines substituted in the 5,5' and 6,6' positions caused the greatest bathochromic shift, those in the 4,4' and 7,7' caused an insignificant deepening of color. Kiprianov and Sych showed [4] that the 5,5' substituted of the disubstituted dimethylthiacarbocyanines showed the greatest bathochromic shift, those substituted in the 4,4' positions, the least. Of the three dihydroxythiacarbocyanines, in comparison to the unsubstituted, the most intensified color was found for the 6,6' hydroxy derivative, the least for the 4,4' substituted [5]. Dimethylamino groups introduced into the 5,5' and 6,6' positions of the thiacyanines and thiapseudocyanines caused an almost identical shift. The same was noticed with 5,5'- and 6,6'-amino and dimethylaminothiacarbocyanines [6].

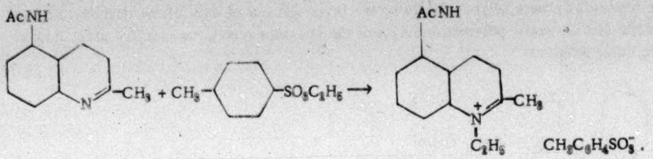
As for investigations into the quinocyanine series, the effect of such substituents as the nitro, amino, acylamino, and dialkylamino groups has scarcely been shown. Hamer [7] synthesized two symmetrically substituted pinacyanols with acetylamino and amino groups in the 6,6' position, and one dye with a nitro group in the para position is known [8].

The effect of the nitro, amino, acetylamino, benzoylamino, and dimethyl groups on the color of quinocarbocyanines was investigated and the effect of disturbance of symmetry of the molecule was shown.

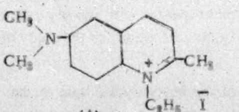
Nitro derivatives of quinaldine were prepared by direct nitration, or by the condensation of the corresponding nitroanilines with paraldehyde [9].

Quaternary salts of 5 and 6-nitroquinaldine were prepared by heating the free bases with methyl iodide or ethyl p-toluenesulfonate, respectively, under pressure. It is necessary to mention that 8-nitroquinaldine could not be made to form the quaternary salt, apparently, because of steric hindrance and basic mutual electronic effects found around the nitrogen of the heterocycle and that of the nitro group.

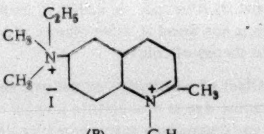
The acylation of the corresponding amino derivatives produced 5-and 6-acetylaminoquinaldine, as well as 5-benzoyl derivatives of quinaldine. Sulfonates of the acylamino derivatives were obtained generally by heating equivalent amounts of the heterocyclic bases with ethyl p-toluenesulfonate.



The condensation of paradimethylaminoaniline with paraldehyde produced 6-dimethylaminoquinaldine, the heating of which in sealed tubes resulted in the separation of two isomeric salts, which differed in their physical and chemical properties. Barbier [10] had observed a similar occurrence.



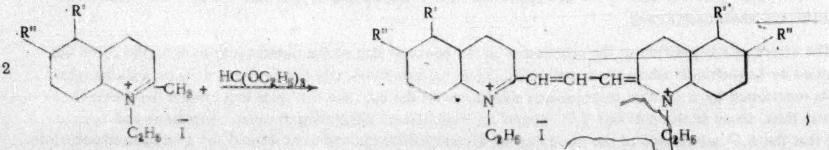
(A)



(B)

Isomer A is less soluble in alcohol, is reddish orange, melts at 226°, and readily condenses with orthoformic ester to form the cyanine dye. The second isomer (B) is yellow-orange, more soluble in alcohol, melts at 100°, and does not give a cyanine condensation with ortho esters. Such properties of these isomeric salts are explained by structural differences.

Symmetrical quinocarbocyanines were prepared by the condensation of quaternary salts with orthoformic ester [11] in pyridine according to the scheme:



where R' and R'' can be $-NO_2$; $-NH_2$; $-NHCOCH_3$; $-NHCOC_6H_5$; $-N(CH_3)_2$.

The absorption spectra of the synthesized dyes are given in Table 1.

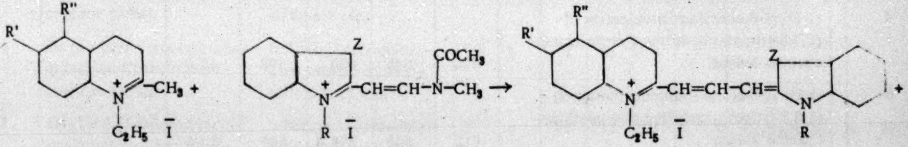
As it is apparent, the nitro group shifts the absorption maximum, as compared to the unsubstituted quinocarbocyanine, toward the longer wavelengths by 26 mμ in the 5,5' positions, by 28 mμ in the 6,6' positions. An amino group in the 6,6' positions of pinacyanol caused a bathochromic shift of 38 mμ. 5,5' Diamino derivatives are interesting. The amino group which, as is known, is a strong auxochrome, on being introduced into the 5,5' positions does not effect the color of the dye. In isocyanines, an amino group in the 6,6' positions shifts the absorption maximum by 20 mμ toward the longer wave lengths, and has no effect on the color in positions 5,5' [7]. Substitution of the hydrogens of the amino group by an acetyl radical causes a hypsochromic shift of 17 mμ, as compared to the amino derivative, but intensifies the color (by 21 mμ) relative to the unsubstituted quinocarbocyanine. Methylation of the p-amino group causes a bathochromic shift of 22 mμ compared to the amino derivative, and by 60 mμ relative to the unsubstituted. This effect for the quinocarbocyanine is in complete agreement with the results for the thiacarbocyanine [12], the bathochromic action of electropositive substituents increases with the increase in the basicity.

TABLE 1

Substituent	Position	Absorption max. in mμ	Shift of absorption max. in mμ
H	–	604	–
NO_2	5	630	26
NO_2	6	632	28
$NHCOCH_3$ . . .	5	616	10
$NHCOCH_3$ . . .	6	625	21
$NHCOC_6H_5$ . . .	5	612	8
NH_2.	5	604	0
NH_2	6	642	38
$N(CH_3)_2$	6	664	60

Substituents which are electronegative in character cause an intensification of the color of the molecules to a smaller extent, as compared to the electropositive. Kiprianov and Pilyugin [13] showed that the absorption maximum of asymmetrical molecules are not always the arithmetical mean values of the corresponding symmetrical ones, but are shifted toward the shorter wave lengths, this shift being greater, the more considerable the difference in the basicity of heterocycles formed by the asymmetrical molecules. Kiprianov and later, Brooker [14] confirmed these phenomena with new examples of cyanine dyes.

Asymmetrical indo-and thiaquinocarbocyanines were synthesized by the condensation of quaternary salts of substituted quinaldine with 2-β-acetanilidovinyl-1,3,3-trimethylindolene iodide and 2-β-acetanilidovinyl-2-methylbenzthiazole ethiodide [15]. The optical data of these dyes are given in Table 2.



+ $C_6H_5NHCOCH_3$

+ HI

Where R' and R" can be: $-NO_2$; $-NHCOCH_3$; $-NHCOC_6H_5$; $-C\langle^{CH_3}_{CH_3}$

R can be: $-CH_3$ or C_2H_5; Z can be: $-S-$ or $-C\langle^{CH_3}_{CH_3}$

The presence of the electronegative nitro group in the 5 and 6 positions of the quinoline ring leads to the equalization of the basicity of the heterocyclic base, as a result of which the absorption maxima of asymmetrical molecules tend to be of additive value (examples 1 and 2). Introduction of an electronegative and electropositive substituent into the molecule of asymmetrical dyes leads to a considerable bathochromic shift of the absorption maximum, relative to the unsubstituted molecule, where it was more expressed in molecules with negative substituents (nitro group).

EXPERIMENTAL

5-Nitroquinaldine methiodide. 2 g of 5-nitroquinaldine and 1.84 g (20% excess) of methyl iodide were placed into a sealed tube. The tube was heated for 3 hours at 60-70° and 2 hours at 100°. Upon raising the temperature at once to 100-110°, a tarring of the reaction mass occurred. At the end of heating, and after cooling, contents of the tube, in the form of a green colored crystalline mass, were transferred into a porcelain dish, triturated with ether, and a small amount of alcohol, filtered, and washed well with ether and alcohol. The salts were purified by two recrystallizations from alcohol. Green crystals, in the form of sheets, which melted at 201° after recrystallization, which corresponded to the literature data [16]. Yield, 58% of the theoretical.

6-Nitroquinaldine ethyl-p-toluenesulfonate. 2 g of p-nitroquinaldine and 2.61 g (20% excess) of ethyl p-toluenesulfonate were heated to reflux for 4 hours on an oil bath at 110-120°. Upon cooling, the quaternary salt was extracted with hot water, and the salt solution was shaken with toluene in a separatory funnel. The aqueous solution of the sulfonate was then evaporated in an evaporating dish on a screen at 150-160°. The sulfonate was stored in a desiccator over sulfuric acid. Upon cooling, the sulfonate solidified into a glass-like mass dark red in color. The sulfonate obtained in this manner readily condensed to the dye; for this reason it was not purified further. Yield of the sulfonate, 1.19 g or 49.70% of the theoretical.

TABLE 2

Expt. No.	Name of dye	Absorption max. in mμ				Shift	
		Symm. I	Symm. II	Asymm. addit.	Asymm. found	Hypsochromic	Bathochromic
1	(1-Methyl-5-nitroquinoline-2)-(1,3,3-trimethylindoline-2)-trimethinecyanine iodide	630	545	587.5	588		0.5
2	(1-Methyl-6-nitroquinoline-2)-(1,3,3-trimethylindoline-2)-trimethinecyanine iodide	632	545	588.5	589.5		1.0
3	(1-Ethyl-5-acetylaminoquinoline-2)-(1,3,3-trimethylindoline)-trimethinecyanine perchlorate.	616	545	580.5	565	15.5	
4	(1-Ethyl-6-acetylaminoquinoline-2)-(1,3,3-trimethylindoline-2)-trimethinecyanine iodide.	625	545	585	570	15.0	
5	(1-Ethyl-5-benzoylaminoquinoline-2)-(1,3,3-trimethylindoline-2)-trimethinecyanine iodide	612	545	578.5	565	13.5	
6	(1-Ethyl-6-aminoquinoline-2)-(1,3,3-trimethylindoline-2)-trimethinecyanine iodide	642	545	593.5	564.5	29	
7	(1-Ethyl-5-nitroquinoline-2)-(3-ethylbenzthiazole-2)-trimethinecyanine iodide	630	558	594	595		1
8	(1-Ethyl-6-nitroquinoline-2)-(3-ethylbenzthiazole-2)-trimethinecyanine iodide	632	558	595	597		2
9	(1-Ethyl-5-acetylaminoquinoline-2)-(3-ethylbenzthiazole-2)-trimethinecyanine iodide	616	558	587	585	2	
10	(1-Ethyl-6-acetylaminoquinoline)-(3-ethylbenzthiazole-2)-trimethinecyanine iodide	625	558	591.5	589	2.5	
11	(1-Ethyl-5-benzoylaminoquinoline-2)-(3-ethylbenzthiazole-2)-trimethinecyanine iodide	612	558	585	582.5	2.5	
12	(1-Ethyl-6-aminoquinoline-2)-(3-ethylbenzthiazole-2)-trimethinecyanine iodide	642	558	600	587	13	

5-Acetylaminoquinaldine ethyl-p-toluenesulfonate. A hydrochloric acid solution of 25 g of 5-nitroquinaldine was added stepwise to a mixture of 40 g of tin and concentrated hydrochloric acid. After several minutes, a crystalline cream-colored residue of the double salt of 5-aminoquinaldine and tin tetrachloride began to separate. Upon cooling the mixture, the residue was filtered, carefully pressed, and dissolved in water. A concentrated sodium hydroxide solution was added to the aqueous solution of the double salt until the precipitation of aminoquinaldine

TABLE 3

Expt. No.	Name of dye	Quaternary salt and its quantity (in g)	$HC(OC_2H_5)_3$, in ml	Condensation conditions		Yield (in %)	M.p.	Found (%)	Empirical formula	Calcd. (%)
				pyridine (in ml)	heating time (min)					
1	Bis-(1-ethyl-5-nitroquinoline-2)-trimethinecyanine p-toluenesulfonate	5-Nitroquinaldine ethyl-p-toluenesulfonate (2 g)	2	6	45	22	324°	S 5.37	$C_{32}H_{30}N_4SO_7$	S 5.21
2	Bis-(1-ethyl-6-nitroquinaldine-2)-trimethinecyanine p-toluenesulfonate	6-Nitroquinaldine ethyl-p-toluenesulfonate (3 g)	3	8	50	21	330	S 4.95	$C_{32}H_{30}N_4SO_7$	S 5.21
3	Bis-(1-ethyl-5-acetylaminoquinoline-2)-trimethinecyanine iodide	5-Acetylaminoquinaldine ethyl-p-toluenesulfonate (4g)	4	7	60	27	262	I 21.84	$C_{29}H_{31}N_4O_2I$	I 21.34
4	Bis-(1-ethyl-6-acetylaminoquinoline-2)-trimethinecyanine iodide	6-Acetylaminoquinaldine ethyl-p-toluenesulfonate (2.5 g)	2.5	6	40	22	320	–	–	–
5	Bis-(1-ethyl-5-benzoylaminoquinoline-2)-trimethinecyanine iodide	5-Benzoylaminoquinaldine ethyl-p-toluenesulfonate (2 g)	2	6	60	12	298	N 7.45-7.63	$C_{59}H_{35}N_4O_2I$	N 7.79
6	Bis-(1-ethyl-6-dimethylaminoquinoline-2)-trimethinecyanine iodide	6-Dimethylaminoquinaldine ethiodide (2 g)	2	6	120	24	242	I 22.73	$C_{29}H_{35}N_4I$	I 22.40

stopped. The base was filtered, washed with water until the alkali was removed; it was then boiled with water and filtered hot. Upon cooling the filtrate, the base crystallized in the form of yellow sheets. The yield of 5-aminoquinaldine after two recrystallizations from water using animal carbon, was 14 g (68.2%). Acetylaminoquinaldine was obtained from aminoquinaldine (4 g) and 6 ml of acetic anhydride by heating for 20 minutes, and was recrystallized from dilute alcohol. Acetylaminoquinaldine, in the form of white needlelike crystals, melted at 204°. The sulfonate was obtained by heating equivalent quantities of acetylaminoquinaldine and ethyl p-toluenesulfonate; the latter, upon condensation with ortho esters, readily gave cyanine dyes.

6-Acetylaminoquinaldine ethyl-p-toluenesulfonate. This preparation was obtained by heating 2.5 g of 6-acetylaminoquinaldine and 2.62 g (5% excess) of ethyl p-toluene sulfonate to 140° with a reflux condenser on an oil bath. Upon cooling, the sulfonate was a solid dark red mass. The salt obtained, as with the subsequently synthesized acetylamino derivative sulfonates, was not purified with water in order to avoid partial hydrolysis of the acyl group. The sulfonate was stored in a desiccator over sulfuric acid. The product readily gave a cyanine condensation.

5-Benzoylaminoquinaldine ethyl-p-toluenesulfonate. 5 g of powdered 5-aminoquinaldine was introduced into 50 ml of a 10% solution of sodium hydroxide, and 5.58 g of benzoyl chloride was added stepwise with efficient stirring to the suspension obtained. The reaction mixture was at all times cooled externally with ice, and was stirred until most of the acid chloride had reacted (after approximately 15 minutes). The reaction mixture was then heated slightly to decompose the benzoyl chloride. Upon cooling the mixture, the precipitate was filtered, washed with water until complete removal of the alkali, and air dried. M.p. 205°. 2 g of benzoylaminoquinaldine and 1.67 g (5 % excess) of ethyl p-toluenesulfonate were heated to 140° for 3 hours with a reflux condenser. The sulfonate salt obtained in this manner was condensed with ortho esters and gave good quinocyanine dyes.

6-Dimethylaminoquinaldine ethiodide. 3 g of 6-dimethylaminoquinaldine and 3.33 g (20% excess) of ethyl iodide was heated for 6 hours in a sealed tube at 140-150°. Upon cooling, the crystalline orange mass was transferred from the tube into a porcelain dish, where it was ground with a small amount of alcohol and ether, filtered, and once

TABLE 4

Expt. No.	Name of dye	Quaternary salt and its quantity (in g)	Intermediate product (in g)
1	(1-Methyl-5-nitroquinoline-2)-(1,3,3-trimethylindolenine-2)-trimethinecyanine iodide	5-Nitroquinaldine methiodide (0.61 g)	2-β-Acetanilidovinyl-1,3,3-trimethylindolenine iodide (0.75 g)
2	(1-Methyl-6-nitroquinoline-2)-(1,3,3-trimethylindolenine-2)-trimethinecyanine iodide	6-Nitroquinaldine methiodide (0.44 g)	Same (0.5 g)
3	(1-Ethyl-5-acetylaminoquinoline-2)-(1,3,3-trimethylindolenine-2) trimethinecyanine iodide	6-Acetylaminoquinaldine ethyl-p-toluenesulfonate (0.85 g)	Same (0.9 g)
4	(1-Ethyl-5-acetylaminoquinoline-2)-(1,3,3-trimethylindolenine-2)-trimethinecyanine perchlorate	5-Acetylaminoquinaldine ethyl-p-toluenesulfonate (0.85 g)	Same (0.9 g)
5	(1-Ethyl-5-benzoylaminoquinoline-2)-(1,3,3-trimethylindolenine-2)-trimethinecyanine iodide	5 Benzoylaminoquinaldine ethyl-p-toluenesulfonate (0.36 g)	Same (0.3 g)
6	(1-Ethyl-5-nitroquinoline-2)-(3-ethylbenzthiazole-2)-trimethinecyanine iodide	5-Nitroquinaldine methiodide (0.45 g)	2-β Acetanilidovinyl-3-ethylbenzthiazole iodide (0.5 g)
7	(1-Ethyl-6-nitroquinoline-2)-(3-ethylbenzthiazole-2)-trimethinecyanine iodide	6-Nitroquinaldine methiodide (0.90 g)	Same (0.1 g)
8	(1-Ethyl-6-acetylaminoquinoline-2)-(3-ethylbenzthiazole-2)-trimethinecyanine iodide	6-Acetylaminoquinaldine ethyl-p-toluenesulfonate (1.56 g)	Same (1.5 g)
9	(1-Ethyl-5-acetylaminoquinoline-2)-(3-ethylbenzthiazole-2)-trimethinecyanine iodide	5-Acetylaminoquinaldine ethyl-p-toluenesulfonate (0.52 g)	Same (0.5 g)
10	(1-Ethyl-5-benzoylaminoquinolidene-2)-(3-ethylbenzthiazole-2)-trimethinecyanine iodide	5-Benzoylaminoquinaldine ethyl-p-toluenesulfonate (0.98 g)	Same (0.8 g)

more ground with ether. Isomer (A) was isolated in the form of dark red crystals by crystallization from a small amount of alcohol.

This isomer formed a cyanine dye with ethyl orthoformate. M.p. 224-226° (with decomp.). Isomer (B), of lighter color, was isolated from the mother liquor by precipitation with ether, which did not form cyanine dyes. M.p. 100°. Upon further heating, the molten salt solidified in the capillary, and melted at 222-225° (with decomp.); it is believed that isomerization to (A) had occurred.

Synthesis of Dyes. Data on the synthesis of dyes and their properties are given in Tables 3 and 4.

Bis-(1-ethyl-6-aminoquinoline)trimethinecyanine iodide. 0.6 g of the dye bis(1-ethyl-6-acetylaminoquinoline-2)trimethinecyanine iodide was saponified by heating with 6 ml of conc. hydrochloric acid for 3 hours on the boiling water bath. Upon cooling, the yellow solution of the saponified dye was neutralized with ammonia. The solution turned green. The precipitate which formed was filtered and washed with water to complete removal of the ammonia. 2 ml of a saturated potassium iodide solution was added to the hot alcoholic solution of the dye. Upon cooling, a dark green powder with a bronze cast separated. The dye was filtered, washed with water, alcohol,

TABLE 4 — (continued)

Reaction condition		Yield (in %)	M.p. with decomposition	Found (in %)	Empirical formula	Calculated (in %)
Pyridine (in ml)	Heating time (in min.)					
5	40	34	258°	I 24.93	$C_{24}H_{24}N_3O_2I$	I 24.72
4	40	60	265-266	I 24.40	$C_{24}H_{24}N_3O_2I$	I 24.72
3	45	27	272-275	I 23.22	$C_{27}H_{30}N_3OI$	I 23.53
4	45	32	228-229	Cl 7.23	$C_{27}H_{30}N_3O_5Cl$	Cl 6.92
2	60	27	230-232	N 6.81, 6.76	$C_{32}H_{32}N_3OI$	N 6.98
3	40	26	273	N 7.83, 7.99	$C_{22}H_{20}N_3O_2SI$	N 8.12
5	45	20	287	I 24.70	$C_{22}H_{20}N_3O_2SI$	I 24.53
8	30	30	308	N 7.34, 7.45	$C_{25}H_{26}N_3OSI$	N 7.73
3	50	25	278	I 23.10	$C_{25}H_{26}N_3OSI$	I 23.10
4	50	24	262	I 20.60	$C_{30}H_{28}N_3OSI$	I 20.96

and ether. M.p. 262° (with decomp.). Yield after recrystallization from alcohol was 42.6% of the theoretical. Absorption maximum, 642 mμ.

(6-Amino-1-ethylquinoline-2)-(1,3,3-trimethylindolenine-2)-trimethinecyanine iodide. 0.3 g of dye No. 3 (Table 4) was saponified by heating with 5 ml of conc. hydrochloric acid for half an hour. Upon heating, the dye dissolved completely with decolorization. The dye was precipitated from the acidic solution with a 15% ammonia solution. The dark green powdery precipitate was filtered, washed with water to complete removal of ammonia, then with alcohol and ether, and then dissolved in boiling alcohol. 2 ml of a potassium iodide solution was added to the hot filtered alcoholic dye solution. After cooling, fine dark green crystals with a bronze cast of the dye separated. Yield of the dye after recrystallization from alcohol, 40%. Absorption maximum, 564.5 mμ. It melted with decomposition within the interval of 188-222°.

Found %: N 8.55, 8.62. $C_{25}H_{28}N_3I$. Calculated %: N 8.45.

(6-Amino-1-ethylquinoline-2)-(3-ethylbenzthiazole-2)-trimethinecyanine iodide. The dye was obtained by the above method. The yield was 55% after recrystallization from alcohol. Fine green crystals. Absorption maximum, 587 mμ.

Found %: N 8.60, 8.57. $C_{23}H_{24}N_3SI$. Calculated %: N 8.38.

SUMMARY

1. The synthesis and investigation of optical properties of several nitro-, amino-, acetylamino-, benzoylamino, and dimethylaminoquinocarbocyanines were effected. Twelve asymmetrical trimethinecyanine dyes, thioquino- and indoquinocarbocyanines, were synthesized, and their properties were investigated.

2. It was shown that all electropositive groups shifted the absorption maximum towards the longer wavelengths, wherein the bathochromic action of the substituent increased with increase in their basicity. Substituents in the 6,6'-positions caused a greater shift than the same in the 5,5'-positions.

3. A hypsochromic shift of the absorption maximum was found with thioquino- and indoquinocarbocyanines with an acetylamino and amino group in the quinoline nucleus, which increased with the increase in the degree of basicity of the heterocycle forming the dye. The thioquinocyanine had a smaller hypsochromic shift than indoquinocyanines with the same substituents in the quinoline nucleus.

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ACTION OF AROMATIC DIAZO COMPOUNDS ON COMPOUNDS OF THE ALKYL ACETOACETIC ESTER TYPE AS A METHOD FOR THE PREPARATION OF ARYLHYDRAZONES OF α-KETO ACIDS, α-AMINO ACIDS, AND NITROGEN HETEROCYCLES

XIV. SYNTHESIS OF 2-CARBOXYINDOLYL-3-ACETIC ACIDS SUBSTITUTED IN THE BENZENE RING AND THE CORRESPONDING INDOLYL-3-ACETIC ACIDS

V. V. Feofilaktov and N. K. Semenova

The investigations of Kögl [1], which showed the chemical nature of heteroauxin as β-indole acetic acid, one of the widely distributed phytohormones, started, on one hand, a search for new methods and improvements in the older ones for the synthesis of β-indolylacetic acid and its derivatives and homologs, and on the other hand extensive investigations into the phytohormones. Although β-indolylacetic acid is of outstanding interest in horticulture as one of the most effective growth factors for the propagation of plant materials by means of grafting, and recently many methods for its synthesis have been developed, it, however, is not a readily available compound. The latter is explained by the poor availability of starting materials for its synthesis (indole, aldehydo- and keto acids), or with comparatively available materials (for example, α-acetoglutaric ester), by the unsatisfactory yields of the intermediate and final products.

Many syntheses of indole acetic acid, known up to 1939 [2] and published later, are accomplished by the introduction of an acetic acid residue into the indole residue. Thus heteroauxin has been synthesized by means of indolyl magnesium iodide by its reaction with chloroacetonitrile [3]; the reaction of indole with diazoacetic ester [4]; from dimethylaminomethylindole (gramine) by the action of HCN or its salts [5]; and others [6,7].

The synthesis of indole derivatives by means of phenylhydrazones which were ring closed with the Fischer reaction, was also accomplished by two variations: either the phenylhydrazones were prepared by the reaction of phenylhydrazine with aldehydo- and keto-acids, or the required phenylhydrazones were obtained by the coupling of phenyl diazonium with compounds of the monoalkyl acetoacetic ester type by the reaction of Japp and Klingemann [8].

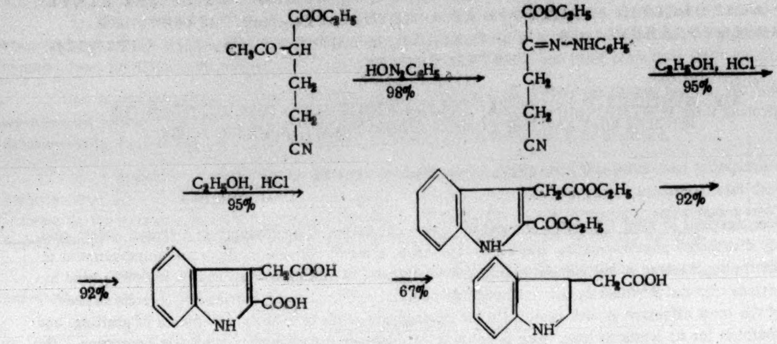
Thus, β-indolylacetic acid was obtained from β-formylpropionic acid and phenylhydrazine [9] (these were first; in addition see: Jackson and Manske [4, 10, 11, 12]); from β-cyanopropionaldehyde acetal [13]; according to a Merck patent [14], ethyl 2,3-dicarbethoxyglutarate phenylhydrazone, obtained from oxalylsuccinic ester, is transformed by the Fischer reaction into ethyl 2,3-dicarbethoxyindolenyl-3-acetate, and by subsequent hydrolysis and decarboxylation into heteroauxin.

By coupling phenyldiazonium with β-cyanoethylacetoactic ester, Keimatsu and Sugasawa [13] synthesized β-cyanomethylpyruvate phenylhydrazone, and from it, ethyl 2-carbethoxyindolyl-3-acetate and the corresponding 2-carboxyindole-3-acetic acid, important intermediate compounds in the synthesis of heteroauxin; they did not, however, prepare the latter. This ester and from it heteroauxin were synthesized by King [15], starting from the relatively available α-aceto glutaric ester.

The coupling reaction of acetoglutaric ester with aryl diazonium for the synthesis of substituted indole derivatives was recently investigated by Findley and co-workers [16]. Tanaka [17] introduced certain improvements into the decarboxylation stage of 2-carboxyindolyl-3-acetic acid into heteroauxin, by converting it initially into the monomethyl ester, i.e., he protected the carboxylic group of the acetate residue.

Of the substituted β-indolylacetic acids, mainly various ester [18], as well as alkyl [19], phenyl [20], and methoxy derivatives [16] are reported in the literature. They all showed smaller physiological activity than heteroauxin [18].

The present investigation was undertaken in order to attempt to improve one of the methods for the synthesis of heteroauxin reported in the literature. The method developed, which followed Keimatsu and Sugasawa's scheme [13], and in the later stage King's [15], was essentially different because, in contrast to these authors, the coupling reaction was conducted in a weakly acidic and neutral reaction medium which gave an almost quantitative yield for this stage; Keimatsu and Sugasawa did not indicate the yield at this stage. In addition, the method reported is simple and practical, since it starts from the readily available acrylonitrile, acetoacetic ester, and aniline (and not phenylhydrazine), and gives high yields of intermediate compounds not requiring purification at any stage.



However, it must be mentioned that the above yields (67%) in the last stage could only be obtained when the decarboxylation was effected with small portions.

Substituted β-indolylacetic acids containing the following substituents in the benzene ring: NO$_2$, SO$_3$H, COOH, Cl, CH$_3$, and others, were synthesized and their physiological activity investigated.

By using aniline and its derivatives, and naphthylamine as the diazo component, in addition to the aryl hydrazones of α-ketoglutaric acids, arylhydrazines of β-pyruvylpropionic, β-cyanomethylpyruvic acids, as well as pyridazine derivatives [26] were obtained, the ability of which to cyclize into the indole ring by heating with alcoholic solutions of sulfuric or hydrochloric acid was investigated. The difference in the ease of cyclization of the indole ring in relation to the nature of the substituent in the aryl hydrazine nucleus was shown (see the Table). Thus, it was observed that arylhydrazones containing electrophylic substituents (NO$_2$, SO$_3$H, COOH, Cl), in the benzene ring required more forcing conditions to close the indole ring then the unsubstituted phenylhydrazones of α-ketoglutaric acid.

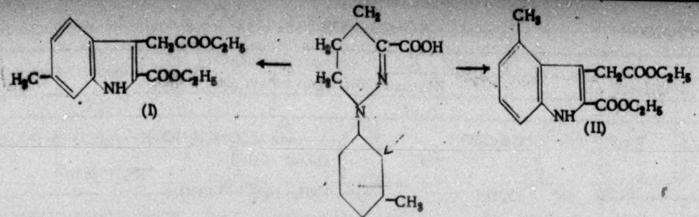
The most hindering effect, as it is apparent from examples of the isomeric o-, m-, p-chlorophenylhydrazones, is caused by a substituent found in the ortho position, somewhat less in the para, and the least in the meta. Conversely, nucleophylic substituents (CH$_3$ group), as well as the unsubstituted naphthalene ring, eased the process of cyclization, and for this reason, tolyl and naphthylhydrazones were converted into indole derivatives under less forcing conditions than unsubstituted phenylhydrazones.

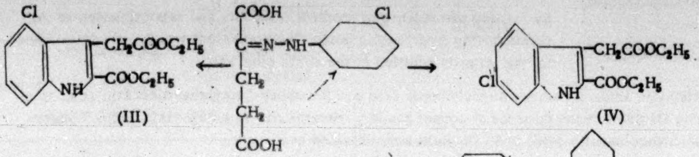
In addition, it was found that the ease and probability of closure of the indole ring was effected by the nature of the radicals of the aliphatic parts of the aryl hyrazones: thus, arylhydrazones of β-cyanomethylpyruvic acid could not be converted into indole derivatives under conditions used, but were readily cyclized into indole derivatives under conditions with which the transformation of the CN group into a carbethoxy was possible.

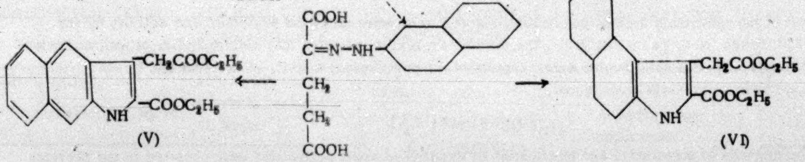
The completion of the cyclization reaction of the indole ring with unsubstituted and o-substituted arylhydrazones was established by the loss of ability of the solution to give the Bülow reaction (for arylhydrazones); while in the case of p- and m-substituted ones, it was established by comparison with the yield of the indole derivatives in experiments with different heating times and concentrations of the alcoholic acid solutions. Only those reactions with the highest yields are reported.

The expected indole derivatives were obtained in the majority of the cases as a result of the above transformations (see Table). In the case of the 4-(K-sulfo)-1-naphthylhydrazone of α-ketoglutaric acid (Formula 13 in Table), the cleavage of the SO$_3$H group and the formation of ethyl 2-carbethoxy-6,7-benzoindolyl-3-acetate occurred, which is normally obtained from α-ketoglutaric acid α-naphthylhydrazone.

During the cyclization of the derivatives of 1-(m-tolyl)pyridazinone-3-carboxylic acid, m-chlorophenylhydrazine, and β-naphthylhydrazine, instead of the two possible products for each separate case (I), and (II), (III)







and (IV), (V) and (VI), only one was isolated. During choice of structure, from the six possible (II), (IV), and (VI) were chosen.

The following reasons were used for the above choices: a) the above discovery of the activating action of nucleophylic derivatives and the deactivating action of electrophylic on the ring closure to the indole nucleus, which agreed with the observations of Köbb [21], Boursche [22]; b) from analogy with the known fact that, upon the condensation of β-naphthylamine with glycerine according to Skraup, the quinoline closes at the α- and not β-carbon atom.

These observations indicated that ring closure occurred at that one of the two possible carbon atoms which has relatively greater density. Such an atom, in the case of m-chlorophenylhydrazone, is the carbon atom found in the para position to the chlorine; in the case of the 1-(m-tolyl)pyridazinone-3-carboxylic acid, it is the carbon atom in the ortho position to the methyl group, and in the case of the β-naphthylhydrazone, the α-carbon atom.

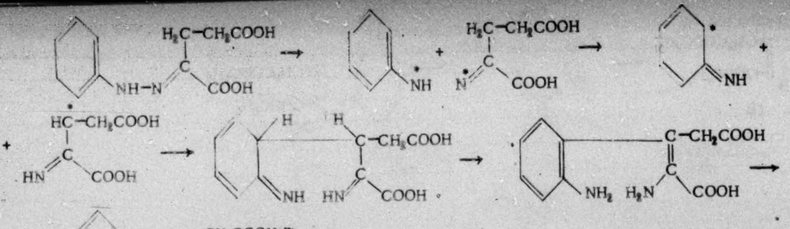
The above, it seems, agrees well with the recently reported views of Pausacker and Schubert [23] on the cyclization of the indole ring Up to now, the accepted scheme for the formation of an indole by the Fischer method is that of Robinson [24], according to which, as it is known, the process occurs by means of the stages a) conversion of the hydrazone into the saturated hydrazine, b) its ortho-benzidine rearrangement to a diamine; c) closing of the pyrrole ring by the cleavage of ammonia from the diamine, i.e., the process consists of subsequent intramolecular rearrangements.

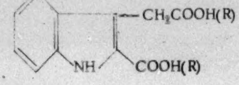
In 1949, Pausacker and Schubert [23] subjected a mixture of equivalent amounts of the o-tolylhydrazone of cyclohexane and 2-methylcyclohexane phenylhydrazone to indole cyclization and obtained a mixture of 4-carbazole derivatives, which led them to conclude that the homolytic cleavage of the $-NH-N=$ bond occurred during the reaction with the formation of radical type intermediate products, the combination of which after the corresponding transformations leads to the carbazole derivatives.

Applying this mechanism of the formation of indole derivatives to α-ketoglutaric acid phenylhydrazone, the following scheme is obtained: (see top of page 672).

For this reason, electrophylic substituents in the ring which attract electrons, among which are those unpaired which result in the combination of separate radicals, will hinder the formation of indole derivatives; conversely nucleophylic substituents which create an increase of electron density will aid in the ring closure, which was indeed observed in the given case.

The esters of substituted 2-carbethoxy-3-indolylaceticacids obtained, in the majority of cases, were characterized





by melting points,nitrogen content, solubility,and saponification to the corresponding dicarboxylic acid. The equivalent weight was determined for the latter in addition to the above constants.

Two of the dicarboxylic acids, 2-carboxy-3-indolylacetic acid and 2-carboxy-3-naphthazoleacetic acid, were decarboxylated by quinoline solutions in the presence of copper powder. Heteroauxin in a 65% yield and 6,7-benzo-indolyl-3-acetic acid (3-naphthazoleacetic acid) in 39.3% yield were obtained as a result.

Part of the substituted 3-carbethoxyindolyl-3-acetic acids were tested for phytohormone activity by the method of E.V. Bobko, N. I. Yakushina [25]. The preliminary results indicated that electrophylic, as well as nucleophilic substituents [18], to a considerable extent suppressed the phytological activity of heteroauxin; however, this subject has not been sufficiently investigated.

EXPERIMENTAL

The methods of preparation and purification of the arylhydrazine derivatives were reported in the previous communication, XIII [26].

Ethyl 2-Carbethoxyindolyl-3-acetate (Formulas 1,2,3, in Table) a) 2.36 g of α-ketoglutaric acid phenylhydrazone (m.p. 153°) was dissolved in 10 ml of absolute alcohol, and the solution, in a round bottomed flask equipped with vertical reflux condenser, was saturated for 5 minutes with dry gaseous hydrogen chloride, passed through a glass tube entering the inner tube of the condenser to the bottom of the flask. The flask was heated on a water bath during the passing of the hydrogen chloride. After 30 minutes, the solution stopped giving the Bülow reaction, and crystals of ammonium chloride formed on the walls of the flask. After pouring into water and ice, colorless crystals of ethyl 2-carbethoxy-3-indoylacetate separated which, after washing with water and drying, weighed 2.6 g, i.e., 94.3% yield, and melted at 82-84° (Formula 1). After recrystallization from aqueous ethyl alcohol the ester melted, in agreement with literature data [13, 15, 27], at 85-86°.

b) 4.85 g of ethyl β-cyanomethylpyruvate phenylhydrazone (m.p. 159°) in 20 ml of 94% ethyl alcohol, in a round-bottomed flask equipped with a reflux condenser, was saturated with hydrogen chloride gas first in the cold and then with heating on the water bath by passing it through the glass tube as in the previous case. Ammonium chloride crystals began to form rapidly on the bottom of the flask. At the end of the heating (after 50 minutes, negative Bülow reaction), the solution acquired a light brown color; after cooling, the contents of the flask were poured into water containing ice (300 ml); the light greyish crystals of the indole derivative were separated, washed with water, and dried. Weight 5.27 g, yield 95.8%, m.p. 80-83°. Recrystallized from aqueous ethyl alcohol with carbon, the colorless needlelike crystals melted at 85-86° (Formula 2).

c) Heating for 30 minutes under these conditions, 1-phenylpyridazinone-3-carboxylic acid (m.p. 172°) with a saturated alcoholic solution of hydrogen chloride, gave ethyl 2-carbethoxyindolyl-3-acetate in a quantitative yield (99.7%)(Formula 3).

2-Carboxyindolyl-3-acetic acid. 1.38 g of ethyl 2-carbethoxyindolyl-3-acetate was heated on the water bath with 10 ml of a 10% aqueous-alcoholic sodium hydroxide solution.* After 10-15 minutes, a thick slurry of the sodium salt formed, which was dissolved in 20 ml of water, acidified with concentrated hydrochloric acid with external cooling by ice. The precipitated, colorless crystals of the acid were filtered, washed with water and dried. Weight 1.0 g, yield 92%, m.p. 234-235° with decomp. Recrystallized from 50% ethyl alcohol, the 2-carboxyindolyl-3-acetic acid, fine colorless, shiny needlelike crystals melted, in accordance to the literature data [15], at 236°(decomp.)

* 40% ethyl alcohol was used to prepare alcoholic alkali solution here and subsequently; in this case, 10 g of NaOH was dissolved in 40 g of 40% alcohol.

Esters of 2-Carbethoxyindolyl-3-acetic acid and 2-Carboxyindolyl-3-acetic Acid

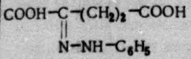
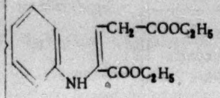
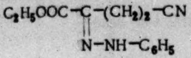
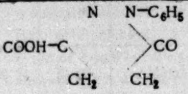
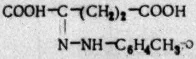
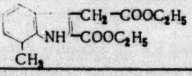
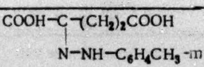
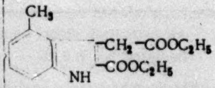
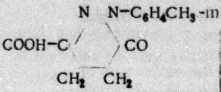
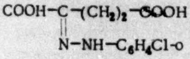
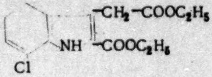
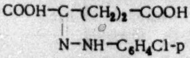
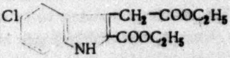
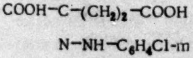
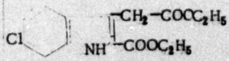
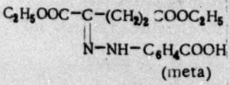
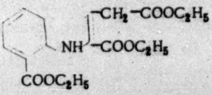
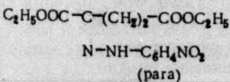
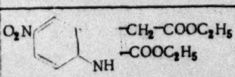
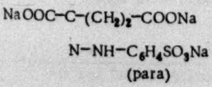
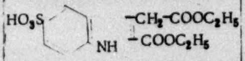
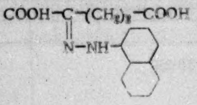
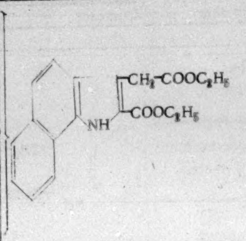
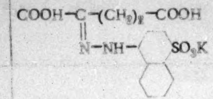
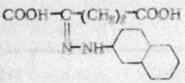
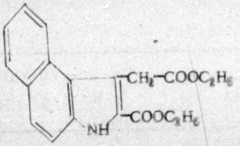
Expt. No.	Starting compound	Conditions for closing indole ring	Esters			Acids	
			Structures	Yield(%)	M.p. (uncor.)	Yield(%)	M.p. (uncor.)
1	2	3	4	5	6	7	8
1	 $COOH-\underset{\underset{N-NH-C_6H_5}{\Vert}}{C}-(CH_2)_2-COOH$	HCl in abs. alcohol; heated 30 min.		94.3	85-86*		
2	 $C_2H_5OOC-\underset{\underset{N-NH-C_6H_5}{\Vert}}{C}-(CH_2)_2-CN$	HCl in aqueous alcohol (94%); heated 50 min.		95.8	85-86	91.3	236*
3		HCl in absolute alcohol, heated 30 min.		99.7	85-86		
4	 $COOH-\underset{\underset{N-NH-C_6H_4CH_3\text{-o}}{\vert}}{C}-(CH_2)_2-COOH$	15% H_2SO_4 in abs. alcohol; heated 6 hours.		95.5	118-119	98.2	218
5	 $COOH-\underset{\underset{N-NH-C_6H_4CH_3\text{-m}}{\vert}}{C}-(CH_2)_2COOH$	10% H_2SO_4 in abs alcohol; heated 10 hours.		A thick, amorphous mass		81	186
5a		10% H_2SO_4 in abs. alcohol; heated 8 hrs.				84.4	186
6	 $COOH-\underset{\underset{N-NH-C_6H_4Cl\text{-o}}{\Vert}}{C}-(CH_2)_2-COOH$	45% H_2SO_4 in abs. alcohol; heated 9 hrs.		86.5	101*	93.6	259-260*
7	 $COOH-\underset{\underset{N-NH-C_6H_4Cl\text{-p}}{\vert}}{C}-(CH_2)_2-COOH$	20% H_2SO_4 in abs. alcohol; heated 9 hrs.		84.1	133-134	96.8	250
8	 $COOH-\underset{N-NH-C_6H_4Cl\text{-m}}{C}-(CH_2)_2-COOH$	20% H_2SO_4 in abs. alcohol; heated 6 hrs.		82.8	146-147	87.1	241
9	 $C_2H_5OOC-\underset{\underset{N-NH-C_6H_4COOH\ (\text{meta})}{\Vert}}{C}-(CH_2)_2\ COOC_2H_5$	50% H_2SO_4 in abs. alcohol; heated 9 hrs.		31.7 (27)	95	95.0	274
10	 $C_2H_5OOC-\underset{N-NH-C_6H_4NO_2\ (\text{para})}{C}-(CH_2)_2-COOC_2H_5$	50% H_2SO_4 in abs. alcohol; heated 4 hrs.		96.2	207	97.7	>350
11	 $NaOOC-\underset{N-NH-C_6H_4SO_3Na\ (\text{para})}{C}-(CH_2)_2-COONa$	60% H_2SO_4 in abs. alcohol; heated 6 hrs.		16.0	146-147	–	–

Table -- (continued)

1	2	3	4	5	6	7	8
12		10% H_2SO_4 in abs. alcohol; heated 16 hrs.		87.0	167-168°	98.0	246°
13		50% H_2SO_4 in abs. alcohol; heated 8 hrs.		23	167-168		
14		10% H_2SO_4 in abs. alcohol; heated 16 hrs.		70.7	210-211	85.2	> 285

Found %: N 6.16,* 6.11. $C_{11}H_9O_4N$. Calculated %: N 6.39.

Indolyl-3-acetic acid (heteroauxin). The decarboxylation of 2-carboxyindolyl-3-acetic acid was effected by King's method [15] slightly modified to increase the yield of the final product.

1.1 g of the above acid was dissolved in 6 g of quinoline, and placed into a Wurtz flask the outlet tube of which was connected with a bent tube fitted underneath an inverted graduated cylinder filled with carbon tetrachloride surrounded by the same liquid in a crystallizing dish. 0.35 g of powdered copper was introduced into the solution, the flask closed with a stopper containing a thermometer going almot to the bottom of the flask, and carefully heated on an oil bath at 170° (internal temperature); there was a rapid evolution of gas bubbles which, however, gradually decreased; a further increase in temperature to 185-195° was required. The latter temperature was kept until the end of the reaction, i.e., the formation of 120 ml of CO_2, which required about 2 hours. The contents of the flask were dissolved in ether (50 ml), after cooling the ether solution was shaken twice with 25 ml of a 10% sodium hydroxide solution. The aqueous alkaline solution was separated, filtered, and acidified with concentrated hydrochloric acid. Without separating the easily precipitated rose colored crystals of the acid, the liquid was twice extracted with hot ethyl acetate (total 50 ml). The solvent was removed, 20 ml of benzene was added to the dry residue, and the mixture refluxed on the water bath for 10 minutes; the hot benzene solution of indolylacetic acid was filtered, transferred to a crystallizing dish, and evaporated; the residue was a substance consisting of rose shiny sheets melting at 162-165°. Weight 0.59 g, yield 67.4% Recrystallized from aqueous alcohol or benzene, almost colorless but soon turning rose in the light, crystals of 3-indolylacetic acid were obtained which melted according to the literature reports [12,15] at 166-167° with decomposition.

Found %: N 7.81, 7.77. $C_{10}H_9O_2N$. Calculated %: N 8.00.

Ethyl 7-Methyl-2-carbethoxyindolyl-3-acetate (Formula 4 in Table). A mixture of 2.5 g of α-ketoglutaric acid o-tolylhydrazone with m.p. 159-160° and 20 ml of 15% alcoholic H_2SO_4 solution was reluxed in a flask for 6 hours (negative Bülow reaction). Upon cooling**, the contents of the flask were poured into a mixture of water and ice; 2.76 g (95.5%) of colorless, scaly crystals melting at 115-117° was isolated by filtration. The substance was readily soluble in methyl and ethyl alcohols, benzene, acetic acid, very soluble in acetone, and insoluble in water. After recrystallization from aqueous alcohol (with the addition of carbon), the ester was a colorless needle-like crystalline substance with m.p. 118-119° without decomposition.

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* The nitrogen in all cases was determined according to the Kjeldahl-Jodlbauer micromethod with the initial reduction of the sample with zinc dust.

** Part of the indole derivative precipitated in the form of crystals.

Found %: N 4.66, 4.58. $C_{16}H_{19}O_4N$. Calculated %: N 4.84.

7-Methyl-2-carboxyindolyl-3-acetic acid. 1.45 g of the ester obtained was saponified with 10 ml of a 10% aqueous alcoholic solution of sodium hydroxide by heating on the water bath for 10-15 minutes. 1.15 g (98.2%) of light yellow crystals, melting at 216-217° with decomposition were obtained on acidifying the cooled and diluted solution with concentrated hydrochloric acid. The crystals were excellently soluble in alcohol, ethyl acetate, acetone, readily in hot acetic acid, and poorly in benzene and ether. On recrystallization from aqueous alcohol, needle-like crystals metling at 218° with decomposition * were obtained.

Found %: N 5.76, 5.67; equiv. 118, 117. $C_{12}H_{11}O_4N$. Calculated %: N 6.00, equiv. 116.5.

4(6?)-Methyl-2-carboxyindolyl-3-acetic acid was prepared by two methods (Formulas 5, 5a). 1.25 g of α-ketoglutaric acid m-tolylhydrazone with m.p. 149° was heated for 10 hours with 15 ml of a 10% alcoholic sulfuric acid solution. A viscous oil separated upon pouring the reaction product into cold water, which gave 0.94 g (81%) of 4-methyl-2-carboxyindolyl-3-acetic acid upon saponification, melting at 186° after recrystallization from aqueous ethyl alcohol. Heating 1-(m-tolyl) pyridazinone-3-carboxylic acid for 8 hours with a 10% alcohol sulfuric acid solution gave 4-methyl-2-carboxyindolyl-3-acetic acid in an 84.4% yield in the form of colorless crystals melting at 186°.

Ethyl 7-Chloro-2-carbethoxyindolyl-3-acetate (Formula 6). 5.4 g of α-ketoglutaric acid o-chlorophenylhydrazone (m.p. 183°) and 44 ml of a 45% alcoholic sulfuric acid solution were heated for 9 hours on the water bath (to a negative Bülow reaction). On cooling, the reaction mixture and the precipitated brown crystals of the indole derivative were poured into ice and water ;the precipitated indole derivative was filtered, washed, and dried; weight 5.36 g, m.p. 96-100°; yield 86.5%.

The substance was very soluble in acetone and ethyl acetate, readily in ethyl and methyl alcohol and acetic acid, and moderately in benzene. After two recrystallizations from ethyl alcohol with carbon, light brown fine crystals of the ester melting at 101° without decomposition were obtained.

Found %: N 4.46, 4.31. $C_{15}H_{16}O_4NCl$. Calculated %: N 4.53.

7-Chloro-2-carboxyindolyl-3-acetic acid. 1.55 g of the ester obtained was saponified with 10% alcoholic sodium hydroxide under the previously reported conditions. 1.18 g (93.6%) of colorless crystals of 7-chloro-2-carboxyindolyl-3-acetic acid was obtained. The substance was moderately soluble in methyl and ethyl alcohols, and in hot glacial acetic acid, poorly in acetone, ethyl acetate, and ether. The acid, recrystallized from ethyl alcohol, melted at 259-260° with decomposition**.

Found %: N 5.28, 5.39; equiv. 124, 125. $C_{11}H_8O_4NCl$. Calculated %: N 5.53; equiv. 126.5.

Ethyl 5-chloro-2-carbethoxyindolyl-3-acetate (Formula 7). 5.4 g of α-ketoglutaric acid p-chlorophenylhydrazone (m.p. 166°) was dissolved in 45 ml of a 20% alcoholic sulfuric acid solution and refluxed for 9 hours on the water bath. Upon slowly cooling the alcoholic solution, part of the indole derivative crystallized in the form of greenish needles melting at 130-132° (without decomposition); the part remaining in the filtrate (m.p. 128-131°) was precipitated upon pouring into water and was filtered. The total yield of the ester was 5.2 g (84.1%). Both portions recrystallized from ethyl alcohol, gave practically colorless fluffy crystals, m.p. 133-134° without decomposition. The ester is excellently soluble in acetone, ethyl acetate, and acetic acid, readily in hot ethyl alcohol and benzene.

Found %: N 4.33, 4.41. $C_{15}H_{16}O_4NCl$. Calculated %: N 4.53.

5-Chloro-2-carboxyindolyl-3-acetic acid. 3.09 g of the ester was saponified with 10% alcoholic sodium hydroxide as in the previous case. 245 g (96.8%) of colorless crystals melting at 247-249° was isolated. The acid is readily soluble in acetone and acetic acid (upon heating), ethyl and methyl alcohols, poorly in ether and ethyl acetate, and insoluble in benzene. Upon recrystallization from alcohol with carbon, the acid melted at 250° with decomposition.

Found %: N 5.38, 5.34; equiv. 124, 123. $C_{11}H_8O_4NCl$. Calculated %: N 5.53: equiv. 126.6.

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* Fox and Bullok obtained the acid by Japp and Klingemann's reaction from acetoglutaric ester in a 6% yield and reported an m.p. 228-229° (corr.) for it [12].

** Fox and Bullok prepared the acid from ketoglutaric acid o-chlorophenylhydrazone in a 31% yield and report an m.p. 253° for it [12].

Ethyl 6-chloro-2-carbethoxyindolyl-3-acetate. (Formula 8). 2.7 g of α-ketoglutaric acid m-phenylhydrazone (m.p. 170-171°) was heated for 6 hours with 30 ml of a 20% alcoholic sulfuric acid solution. Upon cooling the reaction mixture, 1.29 g of shiny light yellow crystals of the indole derivative melting at 135-137° separated. Upon pouring the alcoholic filtrate into water, an additional 1.27 g of crystals with m.p. 125-129° was isolated. Total weight was 2.56 g (82.8%). The substance dissolved readily in alcohol, ether, ethyl acetate, and acetone; it was insoluble in water. After several recrystallizations from ethyl alcohol with the addition of carbon, the ester was obtained in the form of light yellow needle-like or scale-like crystals metling at 146-147° without decomposition.

Found %: N 4.38, 4.45. $C_{15}H_{16}O_4NCl$. Calculated %: N 4.53.

6 Chloro-2-carboxyindolyl-3-acetic acid. 1.55 g of the above ester was saponified with 10% aqueous alcoholic sodium hydroxide solution as previously. 1.06 g (87.1%) of dense rose colored crystals of the dicarboxylic acid melting at 236-237° precipitated upon the acidification of the water-diluted alkaline solution with concentrated hydrochloric acid. The acid dissolved readily in ethyl and methyl alcohols, ethyl acetate, even more so in acetone, was moderately soluble in hot water, and poorly in ligroin and benzene. After a second recrystallization from alcohol, the acid was obtained in the form of light rose colored crystals melting at 241° (with decomposition).

Found %: N 5.40, 5.46; equiv. 125, 126. $C_{11}H_8O_4NCl$. Calculated %: N 5.53; equiv. 126.5.

Triethyl ester of 2,7-dicarboxyindolyl-3-acetic acid. (Formula 9). 3.36 g of diethyl α-ketoglutarate o-carboxyphenylhydrazone (m.p. 104-105°) and 20 ml of a 50% alcoholic solution of sulfuric acid were refluxed for 9 hours on the water bath (to a negative Bülow reaction). The cooled mixture was poured into cold water (150 ml), and the indole derivative extracted with ether. Upon evaporation of the ether, 1.10 g (31.7%) of needle-like crystals melting at 89-91° was obtained. The crystals were very soluble in acetone, ether, ethyl acetate, acetic acid, readily soluble in ethyl and methyl alcohols, and in benzene (upon heating). Recrystallized from aqueous ethyl alcohol with carbon, the triethyl ester of 2,7-dicarboxyindolyl-3-acetic acid was a colorless, light, needle-like crystalline substance melting at 95°. An alcoholic solution of the substance did not combine with alkalies in the cold.

Found %: N 3.80, 3.92. $C_{18}H_{21}O_6N$. Calculated %: N 4.03.

Under an analogous ring closure of the indole ring, 0.94 g (27%) of colorless crystals of the indole derivative was obtained from 2.8 g of α-ketoglutaric acid o-carboxyphenylhydrazone, which was shown to be the triethyl ester of 2,7-dicarboxyindolyl-3-acetic acid (m.p. 95°).

2,7-Dicarboxyindolyl-3-acetic acid. 1.74 g of the ester was saponified by the usual method. 1.25 g (95.0%) of the tricarboxylic acid was isolated in the form of colorless crystals melting with decomposition at 270-272°. The crystals dissolved moderately in alcohol, and acetic acid, poorly in acetone, ethyl acetate, and were insoluble in benzene and ether. Upon recrystallization from ethyl alcohol, colorless needles melting at 274° with decomposition were obtained.

Found %: N 5.09, 5.13; equiv. 86, 85. $C_{12}H_9O_6N$. Calculated %: N 5.32; equiv. 87.7.

Ethyl 5-nitro-2-carbethoxyindolyl-3-acetate (Formula 10). 3.37 g of diethyl α-ketoglutarate p-nitrophenylhydrazone (m.p. 137°) was heated for 4 hours with 40 ml of a 50% alcoholic sulfuric acid solution. The hydrazone dissolved rapidly, and after 30 minutes, crystals of the indole derivative began to separate, the quantity of which increased rapidly, and toward the end of the heating, the contents of the flask were a thick paste. The total yield was 3.08 g, i.e., 96.2%. The substance was moderately soluble in the majority of the organic solvents: alcohols, acetone, ethyl acetate, and poorly in benzene and ligroin. Recrystallized twice from ethyl alcohol, the ester was a weakly rose colored fluffy crystalline substance melting at 207° without decomposition.

Found %: N 8.56, 8.64. $C_{15}H_{16}O_6N_2$. Calculated %: N 8.75.

5-Nitro-2-carboxyindolyl-3-acetic acid. After the saponification of 1.6 g of the ester obtained, 1.29 g (97.7%) of yellow crystals of the acid not melting up to 350° was isolated. The crystals were moderately soluble in hot alcohol and acetic acid, and poorly in ether, benzene, and ligroin. Recrystallized from alcohol, the acid was a light yellow crystalline substance.

Found %: N 10.32, 10.50; equiv. 131, 129. $C_{11}H_8O_6N_2$. Calculated %: N 10.60, equiv. 132.

Ethyl 5-sulfo-2-carbethoxyindolyl-3-acetate (Formula 11). 7.65 g of the trisodium salt of α-ketoglutaric acid p-sulfophenylhydrazone was mixed with 100 ml of a 60% alcoholic solution of sulfuric acid and heated for 6 hours on the water bath. The mineral salts were removed, and the alcoholic filtrate was poured into ice water and left to stand in a cooling mixture. After 40-50 minutes, colorless light crystals of the indole derivative deposited, which weighed 1.14 g (16.0%) after filtration and after standing in the desiccator, and melted at 140-143°. The substance was readily soluble in methyl and ethyl alcohols, acetic acid, ethyl acetate (upon heating), moderately in benzene, poorly in ether, and insoluble in water. Recrystallized from ethyl alcohol (with carbon), the colorless fine crystals melted at 146-147° without decomposition, and gave a qualitative reaction for sulfur.

Found %: N 3.69, 3.76; equiv. 349, 352. $C_{15}H_{17}O_7NS$. Calculated %: N 3.94, equiv. 355.

Ethyl 2-carbethoxy-6,7-benzoindolyl-3-acetate (Formula 12). 2.86 g of α-ketoglutaric acid α-naphthylhydrazone (m.p. 170°) was heated with 40 ml of a 10% alcoholic sulfuric acid solution for 16 hours. Upon the cooling of the solution, light brown shiny, scale-like crystals of the indole derivative crystallized from it. Total weight 2.83 g (87.0%). The substance dissolved readily in acetone, ethyl acetate, and ether, moderately in ethyl alcohol (upon heating), benzene, ligroin, and acetic acid. Recrystallized several times from ethyl alcohol with the addition of carbon, the colorless, (rapidly coloring rose) needle-like crystals of the ester, melting at 167-168° without decomposition, were obtained.

Found %: N 4.43, 4.49. $C_{19}H_{19}O_4N$. Calculated %: N 4.30.

The ester was also obtained by Findlay [16] on a 39% yield (from an azo ester, a product of the coupling of α-naphthylamine with α-acetoglutaric ester); m.p. 167.5-168.5°.

Carboxy-6,7-benzoindolyl-3-acetic acid. 1.63 g of ethyl 2-carbethoxy-6,7-benzoindolyl-3-acetate was saponified with aqueous alcoholic alkali. Upon acidification of the solution, 1.32 g (98.0%) of colorless light crystals of the acid was obtained. The crystals dissolved readily in acetone, acetic acid, and ethyl acetate, and did not dissolve in benzene, ligroin, and water. Recrystallized from alcohol, the colorless, cotton-like, thin, needle-like crystals decomposed on heating at 246°. Findlay reported an m.p. 270° [16].

Found %: N 5.04, 4.98; equiv. 131, 134. $C_{15}H_{11}O_4N$. Calculated %: N 5.20, equiv. 134.5.

6,7-Benzoindolyl-3-acetic acid. 1.34 g of 2-carboxy-6,7-benzoindolyl-3-acetic acid with m.p. 246° was decarboxylated by the method reported for heteroauxin; 0.44 g (39.3%) of the monocarboxylic acid was obtained. The substance was very soluble in acetone, ethyl acetate, readily in ethyl alcohol, somewhat less in methyl alcohol, and poorly in ether; it was insoluble in benzene and ligroin in the cold. Recrystallized from 50% alcohol, the acid was obtained in the form of colorless scale-like crystals melting at 194° with decomposition; Findlay [16] reported an m.p. 194.5°.

Found %: N 5.91, 5.99; equiv. 224, 224. $C_{14}H_{11}O_2N$. Calculated %: N 6.22; equiv. 225.

4.04 g of the 4-potassium sulfonaphthyl-1-hydrazone (Formula 13) was heated with 60 ml of a 50% alcoholic solution of sulfuric acid for 8 hours. The precipitated mineral salts were removed, and the green colored filtrate was poured into ice water. The precipitated greenish blue powder of the indolyl derivative was isolated, washed with water, and dried; it weighed 2.1 g. On dissolving it in ether (100 ml) and upon the slow evaporation of the solution, a small amount (0.75 g) of light violet crystals of the indole derivative crystallized on the wall of the beaker in the form of stars which melted at 157-163°. After washing with alcohol and keeping in a desiccator, the acid did not give a qualitative reaction for sulfur.

After many recrystallizations from alcohol, the indole derivative was obtained in the form of colorless needle-like crystals melting at 167-168° and was found to be ethyl 2-carbethoxy-6,7-benzoindolyl-3-acetate, previously obtained from α-ketoglutaric and α-naphthylhydrazone ; a mixed melting point of both of these preparations did not give any depression.

Therefore, during the process of cyclization of the indole ring, some sort of cleavage of the sulfo group (alcoholysis) occurred to a certain extent; this ester was obtained in a yield of 23%. The main part of the reaction product was found in the bottom of the beaker and was a dark green thick oil giving a positive reaction for sulfur, which was not investigated further.

Ethyl 2-carbethoxy-4,5-benzoindolyl-3-acetate (Formula 14). 2.86 g of α-ketoglutaric acid β-naphthylhydrazone (m.p. 150°) was heated for 16 hours with 40 ml of a 10% alcoholic sulfuric acid solution. The cooled mixture was poured into ice water, and the precipitated light brown flocs of the indole derivatives were filtered, washed with water, and dried. Weight 2.30 g (70.7%), m.p. 200-205°. The substance was readily soluble in alcohol, acetone, ethyl acetate, hot ligroin, and hot benzene. Recrystallized from alcohol with the addition of carbon, and then from ligroin, the ester was obtained as a light brown powder, melting at 210-211°.

Found %: N 4.07, 3.98. $C_{19}H_{19}O_4N$. Calculated %: N 4.30.

2-Carboxy-4,5-benzoindolyl-3-acetic acid. 1.63 g of the ester was saponified by the usual method. The 1.15 g (85.2%) of the acid isolated, recrystallized from alcohol, was a light brown, high-melting (over 285°) powder, soluble in hot acetic acid, ethyl acetate, and acetone, and insoluble in benzene and ligroin.

Found %: N 4.88, 5.02; equiv 130, 132. $C_{15}H_{11}O_4N$. Calculated %: N 5.20; equiv. 134.5.

SUMMARY

1. The conditions for cyclization of the indole ring of aryl hydrazones of α-ketoglutaric acid and several of its analogs were studied.

It was shown: a) that electrophylic substituents on the benzene ring hinder, and nucleophylic, ease the course of the reaction; b) the cyclization process of 4-potassiumsulfo-1-naphthylhydrazone of α-ketoglutaric acid was accompanied by the cleavage of the sulfo group.

2. The method for the preparation of the heteroauxin was improved. The latter was obtained from an easily available material, ethyl β-cyanomethylpyruvate, in high yield at all stages.

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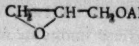
* See Consultants Bureau Translation, p. 463.

REACTIONS OF ETHER OXIDES WITH NITROGEN COMPOUNDS

V. REACTION OF GLYCIDE ETHERS WITH AMMONIA

F. G. Ponomarev

The many investigations of the reactions of ethylene oxide and its closer homologs with nitrogen compounds is reported in detail in the review literature [1-4]. However, there are very few reports [5-7] on the addition of nitrogen compounds to oxides of the type  $\underbrace{CH_2-CH}_{O}-CH_2OAlk$ (glycide ethers). The reactions of methyl, ethyl, isopropyl, and n-butyl glycide ethers with amides were studied. It was shown that the above ether oxides react with formamide and acetamide to form N-mono and N, N-disubstituted amides [8-10]. It was also shown that methyl and ethyl glycide ethers react analogously, but with greater difficulty with ethane- and benzene- sulfonamides [9].

Continuing the investigation in the field of ether oxides, the reaction between methyl and ethyl glycide ethers and ammonia was studied [11]. The experiments showed that, in contrast to the amides whose reaction with the oxides required prolonged heating, methyl glycide ether reacted energetically with ammonia even at room temperature to form the corresponding aminopropandiol ethers (I, II, and III):

$$H_2N-CH_2-CHOH-CH_2OCH_3 \quad \text{(I)} \qquad HN(CH_2-CHOH-CH_2OCH_3)_2 \quad \text{(II)}$$

$$N(CH_2-CHOH-CH_2OCH_3)_3 \quad \text{(III)}$$

The primary amine (I) was isolated in sufficiently pure state, whereas the secondary and tertiary amines (II) and (III) could not be obtained in completely pure form, neither by several vacuum distillations, nor by means of cold absolute ethyl ether in which they had different solubility. The relative yields of each of these aminopropandiol ethers depends on the ratio between the amounts of the glycide ether and ammonia used. With a ratio of 1 1, substances (II) and (III) are mainly obtained; according to the amount of nitrogen in this mixture of (II) and (III), the reaction product contains about 79% of the secondary (II) and 21% of the tertiary (III) amines. With ratios of 1:5, 1:15, and 1:100, the main product is the primary amine (I) in yields of 43, 55, and 64%, respectively, calculated on the ether oxides used.

The ethyl ether of glycide reacts with ammonia in an analogous manner to form, under the reported conditions, a mixture of the corresponding aminopropandiol ethers (IV, V, and VI):

$$H_2N-CH_2-CHOH-CH_2OC_2H_5 \quad \text{(IV)} \qquad HN(CH_2-CHOH-CH_2OC_2H_5)_2 \quad \text{(V)}$$

$$N(CH_2-CHOH-CH_2OC_2H_5)_3 \quad \text{(VI)}$$

The glycide ethyl ether reacts somewhat more slowly with the ammonia than the methyl. This is explained by the fact that it dissolves less readily in ammonia water. The yields of the aminopropandiol ethers from ethyl glycide ether and ammonia were found to be close to the yields of the corresponding ethers from methyl glycide ether. The experimental results showed that glycide ethers reacted with ammonia by the general scheme for the monosubstituted ethylene oxides, and could be placed by their reactivity in the same order as propylene oxide [12,13]. The alkoxy group, apparently has no essential effect on the rupture of the oxide bond.

All of the substances (I-V) possess basic properties and are colorless liquids for the primary amines (I and IV), and solid paraffin-like substances for the secondary (II and V) and tertiary (III and VI), amines. The primary amines (I and IV) were studied in more detail. The acetylation and dehydration of the aminoalcohols (I and IV) obtained were investigated, and picrates, hydrochlorides and phosphates of both these bases were prepared. In addition the chloroaurate and ethiodide of amine (I), and the oxalate of aminoalcohol (IV) were also prepared.

Diacetates were obtained on the acetylation of aminoalcohols (I and IV), which did not contain free hydroxyl groups and did not give a characteristic reaction for the primary amino group. These properties of the diacetates, as well as their constants, mean that both of the groups (hydroxyl and amino) had been acetylated in the aminoalcohols (I and IV). The diacetates can be assigned the formulas (VII) and (VIII):

$$CH_3O—CH_2—CH(OCOCH_3)—CH_2—NHCOCH_3$$

(VII)

$$C_2H_5O—CH_2—CH(OCOCH_3)—NHCOCH_3.$$

(VIII)

Experiments on the dehydration of the aminopropandiols (I and IV) by the action of various dehydration media with the aim of preparing the corresponding ethylene imines did not give satisfactory results, in spite of the widely varied experimental conditions. For example, aminoalcohol (I) was twice subjected to vacuum distillation with powdered potassium bisulfate. However, the splitting out of water did not occur, and the product was almost quantitatively recovered unchanged. The formation of the imine could not be detected in the products of the reaction of the amino alcohol with phosphoric anhydride. In this case the amino alcohol (I) was converted into a substance of the composition $C_4H_9ON \cdot H_3PO_4$. If the dehydration of amino alcohol (I) was effected with phosphoric anhydride in the absence of a solvent, then the product tarred almost completely.

A product of undetermined structure with a lower boiling point was obtained by the action of acids (oxalic and phosphoric) on aminoalcohols (IV).

EXPERIMENTAL

1. Reaction of Methyl Glycide Ether with Ammonia

Synthesis of 3-Methoxypropanol-2-amine (together with S. F. Popov)

a) 10 g of glycide methyl ether (b.p. 110-112°, n_D^{25} 1.4040 [8]) was added in small portions to 50 g of a 25% aqueous ammonia solution. A homogeneous colorless liquid was obtained; the temperature of the reaction mixture rose from 20 to 40°. After standing for 24 hours, the ammonia and water were distilled off from the reaction mixture, and the product distilled first in vacuum and then at normal pressure. 5.1 g (43%) of 3-methoxypropanol-2-amine (I) and 4.9 g of a mixture of the secondary and tertiary amines (II) and (III) which are reported on below, were obtained.

b) Upon mixed 15 g of the ether with 225 g of 25% aqueous ammonia solution under the above conditions, 10 10 g (55%) of 3-methoxypropanol-2-amine (I) and 4 g of a mixture of substances (III and IV) were obtained. Analogous results were obtained on using a 33% solution of ammonia.

c) From 15 g of the ether and 1500 ml of a 25% aqueous solution of ammonia, 11.5 g (64%) of amino alcohol (I) and 3.6 g of the mixture of substances (II and III) were obtained. Therefore, the yield of aminopropanandiol (I) is increased with the increase in the amount of the ammonia used in the reaction.

After redistillation, 3-methoxypropanol-2-amine (I) had the following properties: b.p. 101-103° at 15 mm and 169-171° at atmospheric pressure: d_4^{20} 1.0604; n_D^{20} 1.4590; MR_D 27.11; calculated 27.26. 0.1136 g substance: 10.88 ml 0.1 N. H_2SO_4 (according to Kjeldahl). 0.1578 g substance: 15.15 ml 0.1 N H_2SO_4. 0.1460 g substance: 0.3219 Ag (according to Zeisel). 0.1308 g substance: 12.55 ml 0.1 N. NaOH. 0.1786 g substance: 17.18 ml 0.1 N NaOH. Found %: N 13.41, 13.44; CH_3O 29.10; OH 16.31, 16.19. $C_4H_{11}O_2N$. Calculated %: N 13.33; CH_3O 29.52; OH 16.35.

The methyl ether of aminopropandiol (I) is a colorless liquid with a weak amine odor and basic properties. It dissolves readily in water, alcohol, and acetone, poorly, in benzene; it is insoluble in ether. It rapidly decolorized a solution of bromine in chloroform. It gave the isonitrile reaction with chloroform and the color reaction for the primary amino group with sodium nitroprusside in acetone. It reacted with metallic sodium. It can be stored for a long time, without change, in closed bottles. Under ordinary conditions, it absorbed moisture. A 0.3408 g sample of the substance showed a weight increase of 20, 21, 25, and 34% after 6, 12, 24, and 36 hours, respectively.

The chloraurate of amine (I) was obtained by mixing a hydrochloric acid solution of 0.3 g of the product with an aqueous solution of $AuCl_3$ (1 g). Orange crystals. They crystallized with one molecule of water. They melted at 105-106° after being washed many times with absolute ether.

0.3526 g substance: 0.1510 g Au. Found %: Au 42.80. $C_4H_{12}O_2N \cdot AuCl_4 \cdot H_2O$. Calculated %: Au 42.58.

It must be mentioned that the water of crystallization in the chloraurate is held very strongly, and that it is not removed even upon prolonged heating of a sample in the drying cabinet at 90°.

Amine (I) hydrochloride was prepared by the evaporation of a solution of the product in dilute hydrochloric acid on the water bath. Colorless crystals which liquify in the atmosphere. They melted in a closed capillary at 86-87° after being dried in a desiccator over phosphoric anhydride.

0.2252 g substance: 15.79 ml 0.1 N $AgNO_3$. 0.1583 g substance: 10.50 ml 0.1 N H_2SO_4 (Kjeldahl). 0.1641 g substance: 10.72 ml 0.1 N H_2SO_4. Found %: Cl 24.77; N 9.28, 9.14. $C_4H_{11}O_2N \cdot HCl$. Calculated %: Cl 25.05; N 9.89.

Aminoalcohol (I) picrate was prepared by mixing alcoholic solutions of equimolar quantities of the product and picric acid. After 24 hours, lemon yellow crystals precipitated, which melted at 96-98° after recrystallization from water. It gradually decomposed upon storage in a desiccator over sulfuric acid.

Analysis of the picrate. The sample of the substance and 0.4 g of powdered sulfur in 15 ml of 30% oleum was heated in a Kjeldahl on a boiling water bath for an hour, and the analysis then conducted in the usual manner according to Kjeldahl.*

0.1146 g substance: 13.13 ml 0.1 N H_2SO_4. 0.1014 g substance: 11.56 ml 0.1 N H_2SO_4. Found %: N 16.04, 15.96. $C_{10}H_{14}O_9N_4$. Calculated %: N 16.77.

Base I ethiodide was prepared by mixing equimolecular quantities of the reagents in absolute ether solution. The reaction occurred with the evolution of heat. An oily substance came out on shaking. Upon placing it, after the distillation of the ether, in a desiccator over P_2O_5 for a prolonged period of time, it thickened, assumed the form of a syrup, but it did not crystallize. Before analysis, the product was kept for several days in a desiccator over phosphoric anhydride.

0.1960 g substance: 8.14 ml 0.1 N H_2SO_4 (Kjeldahl). 0.1284 g substance: 5.21 ml 0.1 N H_2SO_4. Found %: N 5.81, 5.66. $C_6H_{16}O_2NI$. Calculated %: N 5.32.

Amine (I) phosphate formed readily upon the evaporation of the solution of 2 g of the product with 1 ml of dilute (1:1) phosphoric acid, d 1.54. After recrystallization from alcohol, colorless scaly crystals with m.p. 154-156° were obtained.

0.1012 g substance: 5.19 ml 0.1 N H_2SO_4. 0.1162 g substance: 6.10 ml 0.1 N H_2SO_4. Found %: N 7.17, 7.35. $C_4H_{11}O_2N \cdot H_3PO_4$. Calculated %: N 6.89.

Acetylation of the aminoalcohol (I) Diacetate (VII) was obtained in the form of a colorless thick liquid with a specific odor by the action of acetic anhydride on 3-methoxypropanol-2-amine.

B.p. 173-175° at 15mm; d_4^{20} 1.1137; n_D^{20} 1.4552; MR_D 46.09; calculated 46.05. 0.1050 g substance: 5.97 ml 0.1 N H_2SO_4 (according to Kjeldahl). 0.1120 g substance: 6.36 ml 0.1 N H_2SO_4. Found %: N 7.96, 7.95. $C_8H_{15}O_4N$. Calculated %: N 7.40.

Diacetate (VII) is readily soluble in water, alcohol, and ether. It does not contain a free hydroxyl group and does not give a positive for a primary amino group with chloroform or with sodium nitroprusside.

Action of potassium bisulfate and phosphoric anhydride upon 3-methoxypropanol-2-amine (I). A series of experiments under various conditions was conducted. Several of these are reported below.

a) 10 g of the aminoalcohol was twice distilled over 8 g of anhydrous finely ground potassium bisulfate at 110° at 25 mm. The product obtained: nitrogen found 11.95 and 12.65%; calculated for the starting substance: $C_4H_{11}O_2N$. %: N 13.13. Therefore, the product practically does not dehydrate under the action of potassium bisulfate, and it was almost quantitatively recovered.

b) 7 g of the product in 20 ml abs. acetone was shaken energetically with 9 g phosphoric anhydride. An evolution of heat occurred. After twenty four hours, the product was heated for 1 hour on the boiling water bath;

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* The picrates were analyzed in an analogous manner in all of the subsequent experiments.

the solution was separated from residue by decantation; filtered, and after the distillation of the acetone, distilled at ordinary pressure. 1 g of a light yellow liquid was obtained at 168-170°, from which a phosphorus-containing substance insoluble in alcohol, ether, acetone, and chloroform was obtained on standing in a desiccator over phosphoric anhydride.

0.1171 g substance: 6.75 ml 0.1 N H_2SO_4 (according to Kjeldahl). 0.1156 g substance: 6.68 ml 0.1 N H_2SO_4. Found %: N 8.07, 8.09. $C_4H_9ON \cdot H_3PO_4$. Calculated %: N 7.56.

Analogous results were obtained upon conducting the experiments in absolute benzene, ether, and chloroform.

c) 6 g of the aminoalcohol was added to 3 g of phosphoric anhydride at room temperature. The reaction proceeded very violently with a great evolution of heat and strong tarring. Upon vacuum distillation at 20 mm, only 0.8 g of substance (the main mass tarred) with b.p. 81-85° in the form of yellowish liquid with an intense ammoniacal odor, readily soluble in water and alcohol, was obtained. Analysis for nitrogen gave a figure which was very close to that obtained in the previous experiment b, i.e., 8.04 and 8.05%. The undistillable residue, a solid tarry product, was not investigated.

Di-(3-Methoxypropanol-2)-amine and Tri-(3-Methoxypropanol-2)-amine (II and III). 10 g of methyl glycide ether was added in small portions to 10 g of 25% aqueous ammonia solution. The ether dissolved immediately, a homogeneous colorless solution was obtained, which was allowed to stand for 24 hours at room temperature. Immediately after the mixing of the reagents, no reaction occurred. After 10-15 minutes, a voilent reaction started, the temperature of the mixture rose from 18 to 75°, the stopper was blown from the neck. If the temperature (25-30°) was regulated by cooling, the reaction proceeded quietly and was completed within 1.5-2 hours. After standing for 24 hours, the ammonia, water, and a small amount of the primary amine (I) distilled from the reaction mixture. Upon vacuum distillation of the residue in the flask, 6.5 g of a mixture of the secondary and tertiary amines (II and III) was obtained in the form of a thick colorless liquid, which slowly solidified and changed into a paraffin like, fatty-to-the-touch, mass melting at 48°.

B.p. 171-175° at 10 mm; 0.1540 g substance: 7.53 ml 0.1 N H_2SO_4 (Kjeldahl). 0.1422 g substance: 6.81 ml 0.1 N H_2SO_4. Found %: N 6.84, 6.71. $C_8H_{19}O_4N$. Calculated %: N 7.24. $C_{12}H_{27}O_6N$. Calculated %: N 4.98.

The above analytical data showed that there was about 79% of the secondary (II) and 21% of the tertiary (III) amines in the mixture obtained. Upon conducting this experiment without cooling, the reverse occurred, the yield of amine(III) increased to 75% and that of product (II) decreased to 25%.

It must be mentioned that the analysis of the mixture of amines (II and III) formed with the main product (I) in all of the above experiments a, b, and c, gave a figure very close to that given in the previous experiment for this mixture of amines (II and III).

0.1048 g substance: 4.87 ml 0.1 N H_2SO_4. Found %: N 6.50.

The mixture of amines (II and III) obtained was readily soluble in water and alcohol, poorly in ether. The aqueous solutions gave an alkaline reaction. They were stored for long periods without change, only a slight yellowing occurred. Because this mixture of amines (II and III) was difficult to separate by vacuum distillation, it was treated with cold ether.

2.6 g of the mixture of amines (II and III) was treated with shaking 5 times with 10 ml of cold (+5°) absolute ethyl ether. The undissolved portion, a 1.5 g quantity, in the form of a colorless paraffin like mass, was transferred to the filter and washed with ether. It was readily soluble in water and alcohol, and gave an alkaline reaction. It melted at 58-60°.

0.1551 g substance: 7.73 ml 0.1 N H_2SO_4 (Kjeldahl) 0.1415 g substance: 6.91 ml 0.1 N H_2SO_4. Found %: N 6.98, 6.84. $C_8H_{19}O_4N$. Calculated %: N 7.24.

1.1 g of the tertiary amine (III) was isolated in the form of a colorless oily substance upon the removal of the ether from the filtrate on the water bath, which partly crystallized on standing. The amine (III) obtained was soluble in water, alcohol, and ether.

0.1212 g substance: 5.05 ml 0.1 N H_2SO_4. 0.1658 g substance: 6.7 ml 0.1 N H_2SO_4. Found %: N 5.83, 5.90. $C_{12}H_{27}O_6N$. Calculated %: N 4.98.

As shown by the analyses, the secondary (II) and tertiary (III) amines, separated from the mixture (II and III) with the ether, were not completely pure and contained small impurities of the other substances.

2. Reaction of Ethyl Glycide Ether with Ammonia

Synthesis of 3-Ethoxypropanol-2-amine (IV) (together with A. A. Aristova)

a) 30 g of ethyl glycide ether [8] (b.p. 128-130°, n^{25}_D 1.4080) was added in small portions, with shaking, to 450 g of 33% aqueous ammonia solution. An increase in temperature from 14 to 22° occurred. Within 20 minutes, the ether layer dissolved and a colorless homogeneous liquid was obtained. After standing for 24 hours, the ammonia and the water were removed, and the product vacuum distilled. 20 g (54.2%) of 3-ethoxypropanol-2-amine, and 8 g of a mixture of the secondary (V) and tertiary (VI) amines, reported below, were obtained.

b) Analogous results were obtained in experiments where a 25% aqueous ammonia solution was used instead of the 33%. Upon using a saturated alcoholic solution of ammonia, as was shown by separate experiments, the yield of amino alcohol (IV) did not exceed 40%, calculated, as in the previous experiments, on the ether oxide. Competely pure 3-ethoxypropanol-2-amine (IV) was obtained on redistillation in vacuum.

B.p. 105-107° at 15 mm; d^{20}_4 1.0360; n^{20}_D 1.4580; MR_D 31.41; Calculated 31.88. 0.2190 g substance: 17.61 ml 0.1 N H_2SO_4 (Kjeldahl). 0.1466 g substance: 0.2862 g AgI (according to Zeisel). 0.2174 g substance: 0.4278 g AgI. 0.0886 g substance: 7.26 ml 0.1 N NaOH. 0.1384 g substance: 11.51 ml 0.1 N NaOH. Found %: N 11.25, 11.65; C_2H_5O 37.50, 37.80; OH 13.93, 14.14. $C_5H_{13}O_2N$. Calculated %: N 11.76; C_2H_5O 37.81; OH 14.27.

The 3-ethoxypropanol-2-amine (IV) obtained was a colorless mobile liquid with a weak amine odor, bitter taste, readily soluble in water, alcohol, and acetone, poorly in benzene and ether. The aqueous solutions gave an alkaline reaction, rapidly decolorized a solution of bromine in chloroform, gave a positive reaction for the primary amino group with sodium nitroprusside and the isonitrile reaction with chloroform, reacted with sulfuric acid. It distilled at 200-202° at normal pressure with a slight decomposition. It absorbed water and carbon dioxide from the atmosphere. A sample of 0.3054 g of the substance gave an increase of 10, 18, 22, and 23% after 6, 12, 24, and 36 hours, respectively.

Amino alcohol (IV) hydrochloride was obtained upon the evaporation of the solution of the product (1 g) in hydrochloric acid (2 ml) on the water bath. The hydrochloride, dried for two days in a desiccator over phosphoric anhydride, was a colorless crystalline substance readily soluble in water and insoluble in ether, which liquified on standing in the air.

0.1245 g substance: 7.82 ml 0.1 N H_2SO_4. 0.1081 g substance: 6.71 ml 0.1 N H_2SO_4. 0.1404 g substance: 9.09 ml 0.1 N $AgNO_3$. 0.1230 g substance: 7.95 ml 0.1 N $AgNO_3$. Found %: N 8.79, 8 69 Cl 23.02, 22.91. $C_5H_{13}O_2N \cdot HCl$. Calculated %: N 9.00; Cl 22.78.

Amine (IV) picrate was a lemon yellow crystalline substance. After recrystallization from water or a mixture of alcohol and ether it melted at 107-109°. It was soluble in water and alcohol. It decomposed gradually upon prolonged standing in a desiccator over sulfuric acid.

0.1062 g substance: 11.88 ml 0.1 N H_2SO_4 (Kjeldahl). 0.1108 g substance: 12.43 ml 0.1 N H_2SO_4. Found %: N 15.66, 15.70. $C_{11}H_{16}O_9N_4$. Calculated %: N 16.09.

Amine (IV) oxalate was obtained on mixing hot alcoholic solutions of equal molecular quantities of the product and anhydrous oxalic acid (m.p. 189°). Colorless prismatic crystals with m.p. 173° (from water).

0.1018 g substance: 4.55 ml 0.1 N H_2SO_4. 0.1054 g substance: 4.83 ml 0.1 N H_2SO_4. Found %: N 6.26 6.41. $C_7H_{15}O_6N$. Calculated %: N 6.69.

Amine (IV) phosphate was obtained upon evaporation of a solution of the product (1 g) with phosphoric acid (0.5 ml), d 1.54, on the water bath. After recrystallization from alcohol, it melted with decomposition at 168 °.

0.1343 g substance: 6.39 ml 0.1 N H_2SO_4. 0.1203 g substance: 5.92 ml 0.1 N H_2SO_4. Found %: N 6.66, 6.88. $C\,H_{16}O_6NP$. Calculated %: N 6.45.

Amino alcohol (IV) did not give a crystalline derivative with either gold chloride or ethyl iodide.

Acetylation of 3-ethoxypropanol-2-amine (IV). Diacetate (VIII) was obtained by the action of freshly distilled acetic anhydride on the amino alcohol in the form of a colorless thick liquid with a specific odor.

B.p. 178-182° at 15 mm; d_4^{20} 1.0884; n_D^{20} 1.4589; MR_D 51.84; Calculated 50.67. 0.1482 g substance: 7.84 ml 0.1 N H_2SO_4. 0.1509 g substance: 8.04 ml 0.1 N H_2SO_4 (according to Kjeldahl). 0.1862 g substance: 0.2194 g AgI (according to Zeisel). Found %: N. 7.41, 7.79; C_2H_5O 22.63. $C_9H_{17}O_4N$. Calculated %: N 6.89; C_2H_5O 22.17.

Diacetate (VIII) was soluble in water, alcohol, and ether. It does not contain a free hydroxyl group and did not give a positive reaction with sodium nitroprusside in acetone and the isonitrile reaction in chloroform.

Action of oxalic and phosphoric acids on 3-ethoxypropanol-2-amine (IV). A series of experiments was conducted; several of these are reported.

a) 4 g of the amine and 2 g of anhydrous oxalic acid (m.p. 189°) were heated in a Claisen flask for 15 minutes at 140° on a paraffin bath. Upon the mixing of the reagents, the temperature rose from 20 to 66°. 1.3 g of the substance was obtained on vacuum distillation in the form of a viscous liquid, bitter to the taste, with an intense ammoniacal odor, readily soluble in water, alcohol, and insoluble in ether.

0.1688 g substance: 6.3 ml 0.1 N H_2SO_4. 0.1840 g substance: 6.6 ml 0.1 N H_2SO_4. Found %: N 5.22, 5.01.

b) a mixture of 4 g of the amino alcohol and 6 ml of phosphoric acid, d 1.54, was stirred at room temperature for 30 minutes and then heated for 3.5 hours on the boiling water bath. Upon mixing the reagents, increase in temperature from 20° to 56° occurred. At the end of the heating, the mixture was diluted with 2 parts of water, and using small separate samples, it was extracted with benzene; or ether, or chloroform; or the sample was saturated with potassium carbonate. However, no reaction product was isolated. The main part of the solution was then treated with a mixture of alcohol and ether. A small amount of an oily substance precipitated.

0.1896 g substance: 6.86 ml 0.1 N H_2SO_4 (Kjeldahl). Found %: N 5.06.

Before the analysis, the product was kept for several days in a desiccator over sulfuric acid.

b) 3 g of the amino alcohol was added dropwise from a funnel to 5 ml of phosphoric acid, d 1.79, heated to 100° in a Claisen flask. Each one of the droplets reacted explosively with the hot phosphoric acid, and white crystals appeared on the walls of the flask. The system was evacuated to 25-30 mm. A very small amount of a substance distilled at 46-50° in the form of a light yellow liquid. The liquid (n_D^{20} 1.3520), dried over potassium hydroxide, was analyzed. Found %: N 2.72 (according to Kjeldahl).

Di-(3-Ethoxypropanol-2)-amine (V) and Tri-(3-Ethoxypropanol-2)-amine (VI). 15 g of ethyl glycide ether was added to 15 g of a 25% aqueous ammonia solution. In contrast to the methyl ether, ethyl glycide ether did not mix with the ammonia immediately; there occurred first a slow, and then a rapid rise in temperature after 30 minutes from 20 to 45°, and the liquid became homogeneous. After 24 hours, the ammonia, water, and a small amount of primary (IV) were distilled off. The residue in the flask weighed 13 g and was a mixture of the secondary (V) and tertiary (VI) amines in the form of a colorless paraffin like mass with basic properties readily soluble in water, and alcohol, poorly in ether; m.p. 61-63°.

0.1486 g substance: 6.29 ml 0.1 N H_2SO_4 (according to Kjeldahl). Found %: N 5.92. $C_{10}H_{23}O_4N$. Calculated %: N 6.33. $C_{15}H_{33}O_6N$. Calculated %: N 4.33.

The above analytical data indicates that there was about 76% of the secondary (V) and 24% of the tertiary (VI) amines in the mixture obtained. The same mixture of the two amines (V and VI) as shown above, was obtained along with the main product (IV) in experiments a and b of section 2.

Since it was very difficult to separate the mixture of amines (V and VI) by vacuum distillation, an attempt was made to separate it by means of ethyl ether, in which their solubilities were difficult.

2.6 g of the mixture of amines (V and VI) was treated 5 times with 10 ml of cold (+5°) absolute ether with shaking. The insoluble part, a 1 g quantity in the form of a light yellow paraffin-like mass, was transferred to the filter and washed with ether. It was readily soluble in water, alcohol, and acetone. Aqueous solutions gave an alkaline reaction. It melted at 91-92°.

0.1047 g substance: 4.54 ml 0.1 N H_2SO_4. 0.1104 g substance: 4.95 ml 0.1 N H_2SO_4. Found %: N 6.07, 6.09. $C_{10}H_{23}O_4N$. Calculated %: N 6.33.

1.6 g of the tertiary amine (VI) was isolated after the removal of the ether from the filtrate on the water bath in the form of a colorless oily liquid which partly crystallized on standing. The amine (VI) obtained was soluble in water, alcohol, and ether.

0.1578 g substance: 5.41 ml 0.1 N H_2SO_4 (according to Kjeldahl). 0.1311 g substance: 4.59 ml 0.1 N H_2SO_4. Found %: N 4.80, 4.90. $C_{15}H_{33}O_6N$. Calculated %: N 4.33.

As the analyses show, the secondary (V) and tertiary (VI) amines isolated from the mixture by means of the ether were not completely pure and contained small contaminants of the other substance.

SUMMARY

1. The reaction between methyl and ethyl glycide ethers and ammonia was studied.

2. It was shown that a mixture of ethers of amino-mono-, di-, and tripropandiol in amounts, the ratio of which depends on the degree of the excess of ammonia, was formed as a result of the reaction.

3. The following products were obtained and characterized: 3-methoxypropanol-2-amine, 3-ethoxypropanol-2-amine, their diacetates and several salts.

4. It was shown, that the aminopropandiol ethers did not give the corresponding ethylene imines by the action of acids (oxalic and phosphoric) and potassium bisulfate, while in the case of the reaction of the amino alcohol (I) with phosphoric anhydride, the substance $C_4H_9ON \cdot H_3PO_4$ was formed.

5. It was pointed out that glycide ethers are not noticeably different from propylene oxide in their reactivity in relation to ammonia.

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* See Consultants Bureau Translation, p. 2135.

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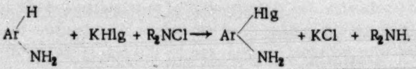
HALOGENATION AND THIOCYANATION OF AROMATIC AMINES WITH LIQUID CHLORAMINES, CHLORAMIDES, ALKYL HYPOCHLORITES, AND ORGANIC HYDROPEROXIDES

A. A. Petrov, G. A. Balaev, and D. B. Ioffe

Complications arising during the direct halogenation of aromatic amines with free halogens (oxidative processes, impossibility of obtaining mono- and in certain cases even dihalides, and impossibility of iodinating directly), and the great practical importance of halogen derivatives of aromatic amines underlined the necessity of developing new methods for the introduction of a halogen into the aromatic ring. A survey of the literature on this question can be found in previous papers by one of the authors [1-4], as well as in recently published texts on methods in organic synthesis [5-7].

Halogenation with oxidizing agents and N-chloramides can be assigned to the number of new methods of halogenation proposed during the past 25 years. As oxidizing agents capable of halogenating aromatic amines in the presence of salts of hydrogen halide acids in acidic media, were proposed hydrogen peroxide, nitric acid, potassium persulfate, iodates, and other substances. Of the chloramides, chloramine-T, N,'- -dichlorourea, N-chloroacetamide, N,N'-dichloropentamethylenetetramine, , and N-chloroimidocarbonic ester were used for this purpose.

The reaction in all cases occurs according to the scheme:

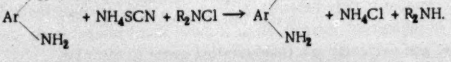


$$\mathrm{Ar}\begin{smallmatrix}\mathrm{H}\\ \mathrm{NH_2}\end{smallmatrix} + \mathrm{KHlg} + \mathrm{R_2NCl} \longrightarrow \mathrm{Ar}\begin{smallmatrix}\mathrm{Hlg}\\ \mathrm{NH_2}\end{smallmatrix} + \mathrm{KCl} + \mathrm{R_2NH}.$$

A development of the chloramide method showed that it was possible to halogenate many aromatic amines with chloramides without side products. This method is of considerable importance because of the simplicity of dosing the halogenating agents so as to obtain mono-, di- and trihalide derivatives with the same or different halogens in the same reaction medium. The complete use of bromine and iodine is another advantage of this method.

Investigation of the mechanism of iodination of aromatic amines with chloramides led to the conclusion that it, apparently, was identical to the method of iodination with oxidizing agents [2]. At the start of the reaction, the oxidizing agent, as well as the chloramide, is consumed in splitting out the iodine. Intense iodination starts only after the separation of the greater part of the iodine into the free state. This peculiarity of the reactions led to the idea that the iodinating agent in all of these cases was hypoiodous acid formed as a result of the oxidation of free iodine by the chloramides or the oxidizing agent. It is possible that the intermediate formation of hypobromous acid occurs during bromination.

In analogy with the method of halogenating aromatic amines, one of the authors was able in 1932 to develop a new method of thiocyanation of aromatic compounds with N-chloramides [8,9]. The reaction occurs according to the following general equation:



$$\mathrm{Ar}\begin{smallmatrix}\mathrm{H}\\ \mathrm{NH_2}\end{smallmatrix} + \mathrm{NH_4SCN} + \mathrm{R_2NCl} \longrightarrow \mathrm{Ar}\begin{smallmatrix}\mathrm{SCN}\\ \mathrm{NH_2}\end{smallmatrix} + \mathrm{NH_4Cl} + \mathrm{R_2NH}.$$

This method was applied successfully in a series of subsequent investigations.

All of the N-chloramides used previously for halogenation and thiocyanation were crystalline substances. There remained the unexplored question of the feasibility of using certain liquid chloramides, especially N-chloramines, most of which are liquid substances, for these purposes. In certain cases, the use of liquid halogenating agents which can be added to the reaction mixture with a burette or microburette, can prove to be more convenient than the use of solid substances.

Also unanswered is the question of the possibility of using alkyl hypochlorites for the purpose of halogenating aromatic amines. These substances are readily prepared from alcohols and in certain cases possess sufficient stability to be kept and used for synthesis as a halogenating agent. Recently a series of papers was published on the halogenation of aliphatic compounds with tertiary butyl hypochlorite [10].

And finally, it seemed of interest to investigate the halogenating properties of organic hydroperoxides.

The solution of the above problems was the aim of this investigation.

As experimental subjects, N-chlorodiethylamine from the chloramines, N-chlorourethane from the liquid chloramides, tert.-butyl hypochlorite from the hypochlorites, and tert.-butyl hydroperoxide from the organic hydroperoxides were chosen. An attempt to use N-chloropiperidine was ended by the instability of this substance.

The halogenation and thiocyanation of aromatic amines with N-chlorodiethylamine were usually conducted in 80% acetic acid in order to counteract the basic character of the diethylamine liberated as a result of the reaction. The chloramine was added dropwise from a microburette to a cooled mixture consisting of the amine, the halide or the thiocyanate and acetic acid, with efficient stirring. The bromination, iodination, and thiocyanation of anthranilic acid, the iodination and thiocyanation of o-toluidine, and the thiocyanation of α-naphthylamine were investigated. The corresponding mono halide or thiocyanate derivatives were obtained in good yields in all of these cases. The oxidation of the amines almost did not occur.

These experiments led to the conclusion that N-chlorodiethylamine can be used successfully for the purpose of halogenating and thiocyanating aromatic amines.

Halogenation with N-chlorourethane was effected in acetic acid, acetone, and methyl alcohol. The best results were obtained in the first one of these solvents. The bromination, iodination, and thiocyanation of anthranilic acid, the thiocyanation of o-toluidine, the thiocyanation of m-toluidine and α-naphthylamine were investigated. This reagent caused a much greater oxidation of the amines in comparison to chlorodiethylamine. The reaction product had to be purified with activated carbon, and for this reason the yields were somewhat lower than in the previous case. Thiocyanation with N-chlorourethane proceed somewhat better than halogenation.

The considerable oxidizing action of N-chlorourethane upon aromatic amines, as well as its strong vessicant action, made work with it difficult, and its application for the halogenation and thiocyanation of aromatic amines limited.

The bromination, iodination, and thiocyanation of anthranilic acid, the bromination of α-naphthylamine, the iodination and thiocyanation of o- and m-toluidine, and the thiocyanation of dimethylaniline with tert.-butyl hypochlorite were attempted. All of these experiments were conducted in acetic acid. Almost all of these experiments were concluded unsuccessfully. Only thiocyanodimethylaniline was obtained in low yield. The hypochlorite energetically oxidized the amines in almost all of the cases, and during the thiocyanation, the ammonium thiocyanate. This substance was found to be quite unsuitable as a halogenating and thiocyanating agent.

The ability of tert.-butyl hypochlorite to thiocyanate dimethylaniline indicates that it liberates free thiocyanogen, which is the thiocyanating agent in this case.

Also unsuitable for the halogenation and thiocyanation of aromatic amines is tert.-butyl hydroperoxide. The bromination iodination, and thiocyanation of anthranilic acid, the iodination and thiocyanation of o-toluidine, and the thiocyanation of dimethylaniline were attempted with this substance. The hydroperoxide reacted very slowly in all cases and mainly as oxidizer of the reagents. Only iodoanthranilic acid and thiocyanodimethylaniline could be isolated in low yield. The last fact is of theoretical interest, since it shows that hydroperoxide can liberate thiocyanogen from ammonium thiocyanate, and evidently is a thiocyanating agent in this case.

Therefore, as the result of the given investigation it was shown that halide amines and haloamides as halogenating and thiocyanating agents for aromatic amines cannot be replaced by other hypohalide compounds, alkyl hypochlorites. They also cannot be replaced with hydroperoxides. As for the haloamines and haloamides, their assortment as halogenating and thiocyanating agents must be considerably widespread. Not only solid, but also liquids, not only chloramides, but also chloramines may be used to halogenate and thiocyanate organic amines, as was shown by the above investigation.

EXPERIMENTAL

1. Halogenation and Thiocyanation with N-Chlorodiethylamine.

N-Chlorodiethylamine was prepared by the action of sodium hypochlorite on diethylamine [11]. A chloramine containing 0.01 g. atom of active chlorine per ml was used for the experiments. This corresponds to approximately 100% concentration.

In all cases, 0.01 mole of the aromatic amine, 0.011 mole of the halide or thiocyanate, and 10-20 ml of acetic acid were used. The mixture was cooled with ice and salt, and a quantity of the chloramine containing 0.011 g. atom of active chlorine was added, with stirring, to it from a microburette. After 0.5-1 hour, the mixture was diluted with water, the reaction product filtered, and recrystallized from aqueous alcohol. The experimental results are listed in Table 1.

TABLE 1

Initial substance	Reaction product	Yield (in %)	Melting point	
			found	literature data
Anthranilic acid	5-Bromo-2-aminobenzoic acid	80	220	220 [12]
	5-Iodo-2-aminobenzoic acid	93	208	210 [12]
	5-Thiocyano-2-aminobenzoic acid	92	170	170 [8]
o-Toluidine	5-Iodo-2-aminotoluene	97	86	87.2 [12]
	5-Thiocyano-2-aminotoluene	60	70	70 [9]
α-Naphthylamine	4-Thiocyano-1-aminonaphthalene	78	142	146-147 [8]

In all cases the reaction products were hardly colored. During iodination, a voluminous separation of iodine occurred which then was absorbed by the iodinated substance.

2. Halogenation and Thiocyanation with N-Chlorourethane.

N-Chlorourethane was prepared by the direct action of chlorine gas on an aqueous solution of urethane. Chlorination of urethane with sodium hypochlorite does not offer any advantages.

The method of halogenation and thiocyanation with this reagent did not differ from that reported above. A chloramide containing 0.01 g. atom of active chlorine in 0.8-1.0 ml was used.

The experimental results are listed in Table 2.

TABLE 2

Initial substance	Reaction product	Yield (in %)	Melting Point	
			found	literature data
Anthranilic acid.	5-Bromo-2-aminobenzoic acid	50	220	220[12]
	5-Iodo-2-aminobenzoic acid	60	210	210[12]
	5-Thiocyano-2-aminobenzoic acid	50	170	170[8]
p-Nitroaniline	2,6-Dibromo-4-nitroaniline	45	200	206[12]
o-Nitrophenol	4-Bromo-2-nitrophenol	74	92	89[12]
o-Toluidine	5-Thiocyano-2-aminotoluene	45	70	70[9]
m-Toluidine	2-Thiocyano-5-aminotoluene	65	83	83[9]
Dimethylaniline	4-Thiocyanodimethylaniline	45	73	74[8]
α-Naphthylamine	4-Thiocyano-1-aminonaphthylene	97	143	146[8]

3. Halogenation and Thiocyanation with Tert.-Butyl Hypochlorite.

Tert.-butyl hypochlorite was obtained by the action of chlorine on a solution of tert.-butyl alcohol and NaOH to a neutral reaction [14]; the substance contained 0.01 g. atom of chlorine in 1.2 ml of the substance, which corresponded to approximately 100% concentration.

Experiments on halogenation with this substance, as was previously mentioned in the introduction, did not give successful results. Intensely colored tars, from which the desired substance could not be crystallized by means of active carbon, were obtained.

Thiocyanation of dimethylaniline gave a light green product in a 10% yield. The substance melted before recrystallization at 70°, after recrystallization from dilute alcohol, at 74°.

4. Halogenation and Thiocyanation with Tert.-Butyl Hydroperoxide.

Tert. butyl hydroperoxide with an activity of 0.01 g. atom of active oxygen in 2 ml was used, which corresponded to approximately 50% concentration.

Iodination of anthranilic acid gave 54% yield of iodoanthranilic acid with m.p. 205° (without recrystallization). The thiocyanation of dimethylaniline produced thiocyanodimethylaniline in a 17% yield, with a m.p. 69° without recrystallization; after recrystallization from alcohol, 74°. The rest of the experiments, as mentioned in the main section, did not lead to the preparation of the expected substances.

SUMMARY

1. The possibility of using N-chlorodiethylamine, N-chlorourethane, tert.-butyl hypochlorite, and tert.-butyl hydroperoxide for the halogenation and thiocyanation of aromatic amines was investigated.

2. It was shown that the first two substances yield monohalogen or thiocyano derivatives of the amines by their actions on solutions of aromatic amines and hydrohalides or thiocyanates in acetic acid.

3. It was shown that tert.-butyl hypochlorite and hydroperoxide can not be used under these conditions for the halogenation and thiocyanation of aromatic amines.

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SYNTHESIS OF SUBSTITUTED CYSTEINES

I. THE POSSIBILITY OF USING DIPHENYLGLYCOLIC ALDEHYDE AND DIPHENYLACETALDEHYDE FOR THE SYNTHESIS OF β,β-DIPHENYLCYSTEINE

T. A. Favorskaya and L. A. Remizova

Dimethylcysteine, or penicillamine, is a necessary starting product for the synthesis of penicillin; at the present time there is an entire series of proposed methods for its preparation [1,2,3,4,5,6].

Attempts to synthesize analogs of β,β-dimethylcysteine containing phenyl groups instead of methyl groups are of unquestionable interest. It was decided to use diphenylglycolic aldehyde as the starting product for the synthesis of β,β-diphenylcysteine. Glycolic aldehyde was used by Fischer and Leuchs [7] for the synthesis of serine, α-amino-β-hydroxypropionic acid by Strecker's method [8], from which cysteine was obtained by Fischer and Raske [9] by the action of phosphorous pentachloride followed by treatment of the compound obtained by $Ba(OH)_2$

In view of the inconvenience of Strecker's method which uses the action of ammonia and free strong acids, the method of N. D. Zelinsky and G. L. Stadnikov [10] was used for the synthesis of α-amino-β-hydroxy β,β-diphenylpropionitrile, who prepared α-aminophenylacetic acid by the action of KCN and NH_4Cl on benzaldehyde in a ligroin solution in the presence of 0.5 ml of water. The authors recommend this method for working with benzaldehyde instead of the usual one of reacting aldehydes with a mixture of KCN and NH_4Cl in aqueous alcoholic solution [11], since in this case they avoided the tarring of benzaldehyde which occurred in an aqueous alcoholic medium.

The starting diphenyl glycolic aldehyde was prepared by a method developed by S. N. Danilov [12]. Benzaldehyde was reduced in an alcoholic solution by zinc and hydrochloric acid to hydrobenzoin. Hydrobenzoin was converted into diphenylacetaldehyde by heating with crystalline oxalic acid; from it diphenyl glycolic aldehyde was obtained by bromination and subsequent hydrolysis. In order to convert this aldehyde into α-amino-β-hydroxy-β,β diphenylpropionitrile, it was dissolved in ether and added to a mixture of equimolecular quantities of KCN and NH_4Cl. 0.5 ml of water was added to the reaction mixture, placed in a bottle with a ground-in stopper. The nitrile formed was not isolated in the free form, but was hydrolyzed at once with 20% hydrochloric acid by heating for 1-2 hours. A mixture of acids was obtained. One of these was found to be β,β-diphenylpyruvic acid, the other, diphenylacetic.

The formation of β,β-diphenylpyruvic acid was explained by the dehydration of β,β-diphenylglyceric acid obtained on the hydrolysis of the nitrile. From the literature [13] it is known that β,β-diphenylglyceric acid dehydrates readily in acidic medium, while the β,β-diphenylpyruvic acid formed evolves carbon dioxide upon heating and is transformed into diphenylacetic acid.

Authentic β,β-diphenylpyruvic acid and its 2,4-dinitrophenylhydrazone were synthesized [14,13]. A mixed melting point determination with the hydrazone obtained above gave no depression. The same mixture of acids was obtained upon the hydrolysis of the nitrile in an alkaline medium with a 25% solution of potassium hydroxide; in addition a decomposition of the nitrile molecule with the formation of benzhydrol occurred. In both experiments, in addition to the above products, the starting diphenylglycolic aldehyde was detected.

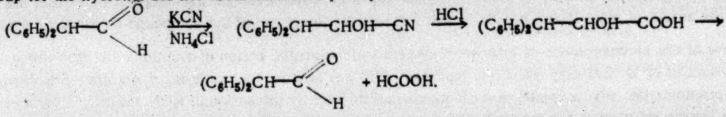
The results of the hydrolysis, therefore, showed that the reaction of diphenylglycolic aldehyde with KCN and NH_4Cl, under the above conditions, did not lead to the formation of the aminohydroxynitrile, but stopped with the formation of the dihydroxynitrile. Subsequent experiments were conducted with double quantities of KCN and NH_4Cl. Diphenylglyceric nitrile was isolated from the reaction products in a yield of 60% of the theoretical.

Upon the hydrolysis of the nitrile in acidic and alkaline media, the same products as in the first experiments were obtained. Therefore, under these conditions, in spite of the great concentration of ammonia, the amino group could not be introduced into the hydroxynitrile molecule.

Then it was decided to try and approach the synthesis of β,β-diphenylcysteine in another manner: by the action of KCN and NH_4Cl on diphenylacetaldehyde to obtain the α-aminonitrile of β,β-diphenyl propionic acid, to convert it to the amino acid, to substitute the hydrogen on its CH group by a bromine, and then by a mercaptan group.

Diphenylacetaldehyde was treated with KCN and NH_4Cl under the same conditions as for diphenylglycolic aldehyde. The reaction product was vacuum distilled, and more than half of the diphenylacetaldehyde used in the reaction distilled off; the undistilled part crystallized, but a substance with a sharp melting point could not be isolated from it even after many recrystallization from alcohol. Analysis of the product obtained showed that it was about 60-70% β,β-diphenyllactonitrile. Upon hydrolysis with 20% hydrochloric acid, only diphenylacetaldehyde and an insignificant amount of a neutral substance with m.p. 192°, which was not investigated further, were obtained.

It is known [15] that α-hydroxyacids can be cleaved into aldehydes and formic acid on being heated with dilute mineral acids. The formation of diphenylacetaldehyde as a result of the hydrolysis of the nitrile obtained shows that this nitrile is α-hydroxy-β,β diphenylpropionitrile; therefore, in this case also, the substitution of the amino group for the hydroxyl did not occur with the hydroxynitrile formed.

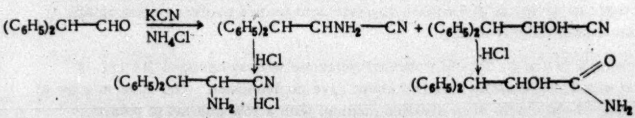


$$(C_6H_5)_2CH-CHO \xrightarrow[NH_4Cl]{KCN} (C_6H_5)_2CH-CHOH-CN \xrightarrow{HCl} (C_6H_5)_2CH-CHOH-COOH \longrightarrow (C_6H_5)_2CH-CHO + HCOOH.$$

The results of the experiments conducted showed the instability of the molecules being studied, which contained two phenyl groups and a hydroxyl group on one and the same carbon atom. The instability of this type of compound was also observed during a study of the reaction of methylphenyl- and diphenylallyl carbinols with dilute sulfuric acid with heating. Under these conditions, methylphenylallylcarbinol gave 27% of acetophenone, and diphenylallylcarbinol decomposed with the formation of 70% of benzophenone [16].

Not obtaining satisfactory results using the above method of N. D. Zelinsky and G. L. Stadnikov, it was decided to return to another modification of their method [11], to a treatment of an ether solution of the aldehyde with an aqueous solution of KCN and NH_4Cl. Diphenylacetaldehyde was first used for reaction. At the end of the reaction, the ether solution was separated from the aqueous solution, and on cooling, a stream of dry hydrogen chloride was passed through it; a rapid precipitation of the hydrochloride of α-amino-β,β-diphenylpropionic acid occurred. From the hydrogen chloride saturated ether solution, after the removal of the salt, a substance was separated which was found to be β,β-diphenyllactamide.

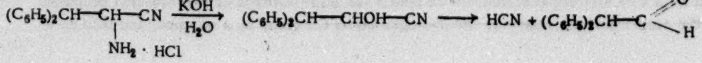
Therefore, in the aqueous thereal solution the reaction proceeded in two directions, to the formation of the aminonitrile (yield 6-8%) and to the formation of the hydroxynitrile (10-15%):



$$(C_6H_5)_2CH-CHO \xrightarrow[NH_4Cl]{KCN} (C_6H_5)_2CH-CHNH_2-CN + (C_6H_5)_2CH-CHOH-CN$$
$$\downarrow HCl \qquad\qquad \downarrow HCl$$
$$(C_6H_5)_2CH-CH(NH_2\cdot HCl)-CN \qquad (C_6H_5)_2CH-CHOH-CONH_2$$

The hydrochloride of the aminonitrile was subjected to hydrolysis in acidic and basic media. Heating it with a 20% solution of hydrochloric acid led to tarring.

R. Fittig's method [17], hydrolysis with a mixture of ether and concentrated hydrochloric acid in the cold, which was used by him for nitriles of unsaturated hydroxy acids, did not lead to satisfactory results. As a result of the hydrolysis of the hydrochloride with a 25% solution of potassium hydroxide, a liquid with an unpleasant odor reminiscent of isonitriles was obtained; the substance gave neutral reaction, and a silver mirror by the action of an ammonial silver oxide solution. A 2,4-dinitrophenylhydrazone was obtained from it, which was identical with that obtained from authentic diphenylacetaldehyde. The substance with the unpleasant odor was present as a very insignificant impurity, since after the preparation of the 2,4 dinitrophenylhydrazone, the odor almost completely vanished. The formation of diphenylacetaldehyde, upon the alkaline hydrolysis of the hydrochloride of the aminonitrile, can be explained by the cleavage of the elements of HCN from the molecule of the hydroxynitrile, arising from the substitution of the amino by a hydroxyl:



$$(C_6H_5)_2CH-CH(NH_2\cdot HCl)-CN \xrightarrow[H_2O]{KOH} (C_6H_5)_2CH-CHOH-CN \longrightarrow HCN + (C_6H_5)_2CH-CHO$$

As it was stated above, in addition to the hydrochloride of the aminonitrile, β,β-diphenyllactamide was isolated from the products of the reaction between diphenylacetaldehyde and KCN and NH_4Cl in aqueous ether solution. The amide was converted into the free β,β-diphenyllactic acid (yield 30-40%). For a mixed melting point determination, authentic β,β-diphenyllactic acid was synthesized by Weise's method [18]. Weise hydrolyzed the nitrile formed by the action of dilute hydrochloric acid upon heating, and obtained a mixture of substances. The hydrolysis of the nitrile was effected by the authors by the action of concentrated hydrochloric acid in ether in the cold.

By the reaction of an ether solution of diphenylglycolic aldehyde with an aqueous solution of KCN and NH_4Cl, the α-amino-β hydroxynitrile of β,β diphenylpropionic acid was isolated in the form of the hydrochloride, the hydrolysis of which was not studied in view of the small yield.

EXPERIMENTAL

Preparation of Diphenylglycolic Aldehyde

Diphenylglycolic aldehyde was prepared by S. N. Danilov's [12] method from bromodiphenylacetaldehyde. An oil and a crystalline product with m.p. 162° were obtained. Both substances gave the same semicarbazone with m.p. 241-242° (from alcohol). The oil gave the semicarbazone readily, upon shaking with a solution of semicarbazide; the crystalline product reacted with this solution only upon heating for 2 hours on the water bath. The liquid aldehyde was distilled at various pressures: at 8 mm the aldehyde did not distill, at 4 mm it distilled but the temperature was not constant, since the distillation was accompanied by the decomposition of the product. Diphenylglycolic aldehyde boiled at 142-143° on distillation in a high vacuum. Yield 65.5% based on the diphenylacetaldehyde. After distillation, the substance crystallized at once, m.p. 52-53°. Upon shaking with a solution of semicarbazide, it gave a semicarbazone with a m.p. 241-242° at once. A mixed melting point determination with the previously obtained semicarbazone did not give a depression. Thedistilled aldehyde was readily soluble in benzene, ether, alcohol, chloroform, while the substance with m.p. 162° dissolved in these solvents only upon heating.

0.0797 g substance: 0.2315 g CO_2; 0.0395 g H_2O. 0.0829 g substance: 20.76 g benzene: Δt 0.095°. 0.0709 g substance: 6.5 ml CH_4 (22°, 760 mm). Found %: C 79.21; H 5.54. M 210.5; number of active hydrogens: 0.936. $C_{14}H_{12}O_2$. Calculated %: C 79.22; H 5.66; M 212; number of active hydrogens 1.

Therefore, according to the analytical results, the substance with m.p. 52-53° is the monomeric form of diphenylglycolic aldehyde, obtained previously, while the substance with m.p. 162° is the product of its polymerization [12].

Preparation of α-Amino-β-hydroxy-β,β-diphenylpropionic Acid by N.D. Zelinsky's Method [10].

13 g of diphenylglycolic aldehyde was dissolved in 100 ml of absolute ether. 4.5 g of powdered KCN, 3.7 g of NH_4Cl, and 0.5 ml of water were added to the ether solution placed in a bottle with a ground-in stopper. Such a quantity of water, according to the author, is completely sufficient since it acts as a catalyst. The reaction mixture was allowed to stand at room temperature for 5-6 days, while the bottle was shaken from time to time. 1-2 hours after the start of the reaction, the separation of a white precipitate began, which gradually filled the whole bottle, and the evolution of ammonia occurred simultaneously. When the amount of the precipitate stopped increasing, the reaction was stopped, although the formation of a silver mirror showed that all of the aldehyde had not reacted. The reaction product was extracted with absolute ether. Part of the solution was used for the preparation of the hydrochloride. A stream of dry hydrogen chloride was passed through the cooled ether solution for 3 hours; however no hydrochloride precipitated, which indicated that an amino group was absent from the reaction product. The ether was removed from the rest of the ether solution; 13.5 g of a thick yellow oil was obtained as a residue; it gave a positive qualitative reaction for nitrogen, a silver mirror by the action of an ammoniacal silver oxide solution, and a semicarbazone identical to that of diphenylacetaldehyde. The nitrile obtained was not isolated in the free form, but was hydrolyzed at once by boiling with 50 ml of 20% hydrochloric acid for 1 hour. A crystalline substance with m.p. 108-114° came out from the cooled solution, which did not give a qualitative reaction for nitrogen.

After several recrystallizations from aqueous alcohol, the melting point increased to 142-144°. The substance gave an acid reaction, sublimed, the sublimate melted at 145-146° and did not give a depression in melting point when mixed with authentic diphenylacetic acid.

0.1076 g substance: 5.95 ml NaOH (T 0.003279). 0.1323 g substance: 0.0436 g Ag. Found: E 224.3; % Ag 32.92. $(C_6H_5)_2CHCOOAg$. Calculated %: Ag 33.85. $(C_6H_5)_2CHCOCOOAg$. Calculated: % Ag 31.12. $C_{14}H_{12}O_2$. Calculated E 212. $C_{15}H_{12}O_3$. Calculated E 240.

Therefore, the substance obtained was a mixture of diphenylacetic and diphenylpyruvic acids. Upon treatment of this mixture with a solution of 2,4-dinitrophenylhydrazine, the 2,4-dinitrophenylhydrazone of diphenylpyruvic acid with m.p. 202-203° was obtained.

0.0505 g substance: 5.9 ml N_2 (19.5°; 756 mm). Found %: N 13.26. $C_{21}H_{16}O_6N_4$. Calculated %: N 13.33.

To obtain the pure silver salt of diphenylacetic acid, the mixture of acids was dissolved in dilute ammonia by heating on the water bath, the excess of ammonia was removed, and a solution of $AgNO_3$ added to the cooled filtered solution. The precipitate salt was washed and dried in a desiccator.

0.1240 g substance: 0.0420 g Ag. Found %: Ag 33.87. $C_{14}H_{11}O_2Ag$. Calculated %: Ag 33.85.

Therefore, upon heating in an ammonia solution on the water bath, diphenylpyruvic acid was completely transformed into diphenylacetic acid.

The hydrolysis of the nitrile was also effected in an alkaline medium. 10 g of the nitrile in 50 ml of a 25% KOH solution (30 ml of water and 20 ml of alcohol) was heated on the water bath for a half hour. The precipitated oily layer was dissolved in ether and dried with fused Na_2SO_4. The liquid obtained on the removal of the ether, crystallized partly. The crystals gave neutral reaction, the test for nitrogen was negative; melting point (from petroleum ether) 65-66°. A mixed melting point with authentic benzhydrol gave no depression. 1 g of pure benzhydrol was obtained. The liquid remaining after the removal of the benzhydrol, gave a semicarbazone with m.p. 238-239° which did not give a depression in melting point upon mixing with the semicarbazone of authentic dephenylglycolic aldehyde.

A small amount of an acid with m.p. 112-114° was obtained from the aqueous solution from the hydrolysis after acidification with sulfuric acid, which did not give a depression in melting point upon mixing with the semicarbazone of authentic diphenylpyruvic acid.

The attempt to synthesize α-amino-β-hydroxy-β,β-diphenylpropionic acid was repeated once more, wherein a double quantity of KCN and NH_4Cl was used for the reaction: for 16.5 g of the aldehyde, 10 g of KCN and 9.2 g of NH_4Cl; the rest of the conditions remained the same. After end of the reaction and the removal of the solvent, the substance obtained crystallized rapidly; after removal of the crystals, anoily liquid remained; no hydrochloride was obtained upon passing hydrogen chloride through its ether solution. The crystalline substance was recrystallized from aqueous alcohol or carbon tetrachloride; m.p. 97-98°. Weight of the pure product, 11.7 g or 62.8% based on the nitrile of β, β-diphenylglyceric acid.

0.0913 g substance: 4.8 ml N_2 (21°, 758 mm). 0.0620 g substance; 16.72 g benzene: Δt 0.08°. 0,0532 g substance: 10.9 ml CH_4 (18.5°, 761 mm). Found %: N 5.94; M 238, number of active hydrogens 1.98. $C_{15}H_{13}O_2$. Calculated %: N 5.85, M 239, number of active hydrogens, 2.

Hydrolysis of β,β-diphenylglyceric acid nitrile was effected in acidic and alkaline media under various conditions in order to try to obtain diphenylglyceric acid.

1) 2 g of the nitrile, 100 ml of 20% hydrochloric acid were heated to boiling for 1 hour. 1.3 g of diphenylacetic acid with m.p. 145-146° was obtained; 70% of theoretical.

2) 1 g of the nitrile, 100 ml of 20% hydrochloric acid were heated on the water bath for 1 hour. 0.8 g of the nitrile was recovered unchanged; in addition, a substance with m.p. 110-141° was isolated, which gave a 2,4-dinitrophenylhydrazone with m.p. 202-203°; a mixed m.p. determination with β,β-diphenylpyruvic acid 2,4-dinitrophenylhydrazone did not give a depression.

3) 2 g of the nitrile, 100 ml of 20% hydrochloric acid were heated on the water bath for 2 hours. 1.4 g of diphenylacetic acid with m.p. 145-146° and 0.1 g of a substance with m.p. 115-131°, a mixture of diphenylacetic and diphenylpyruvic acids, was obtained.

4) 1 g of the nitrile of diphenylglyceric acid, 100 ml of 20% hydrochloric acidwere stirred for 4 days at room temperature. The substance was recovered unchanged.

5) 1 g of the nitrile, 50 ml of a 25% KOH solution were heated on the water bath for a half hour. 0.5 g of benzhydrol with m.p. 66-67° and 0.05 g of the pyruvic acid with m.p. 113-115° was obtained.

In order to compare the diphenylpyruvic acid obtained with an authentic sample, a synthesis of this acid was undertaken [13,19].

Preparation of α-Amino-β,β-diphenylpropionitrile

50 g of diphenylacetaldehyde was dissolved in 100 ml of ether. The solution was placed in a bottle with a ground-in stopper, and 25 g of KCN, 20.5 g of NH_4Cl (1.5 moles), and 0.5 ml of water was added to it. The bottle with reaction mixture was allowed to stand for two week; it was shaken from time to time. After two weeks the solution, giving a positive reaction for the aldehyde group, was separated from a residue which was extracted with ether, and both solutions dried with Na_2SO_4. The aminonitrile was not obtained, since on passing HCl through part of the ether solution obtained, a precipitate of the hydrochloride did not form. The oil remaining after the removal of the ether, was vacuum distilled; 27 g of a substance with b.p. 155° at 7 mm was isolated, which was found to be diphenylacetaldehyde. Its semicarbazone with m.p. 157-158° did not give a depression in melting point on being mixed with authentic diphenylacetaldehyde semicarbazone. The thick mass remaining after the distillation of the aldehyde, solidified on cooling and formed a crystalline substance after the addition of ether, which contained nitrogen. The substance was recrystallized several times from alcohol, but a sharp melting point could not be obtained: m.p. 114-120° which showed that the substance was a mixture. Quantity 9g. The same was shown by the results of the determination of the percent nitrogen, molecular weight, and number of hydroxyl groups.

0.0831 g substance: 2.8 ml N_2 (16°, 772 mm). 0.1629 g substance; 20.19 g benzene: Δt 0.13°. 0.0523 g substance: 2.5 ml CH_4 (16.5°, 751 mm). Found%: N 4.01. M 318.4; number of hydroxyl groups 0.4347. $C_{15}H_{13}ON$. Calculated %: N 6.27. M223; number of hydroxy groups 1.

The substance obtained was hydrolyzed in an acidic medium: 2 g of the substance with m.p. 114-120°, 100 ml of hydrochloric acid were heated to boiling for 1 hour with stirring. The reaction products were extracted with ether, and the extract dried with Na_2SO_4. After the removal of the ether, the residue was vacuum distilled; 1.2 g of a substance with b.p. 149° at 4 mm was obtained, which gave a semicarbazone with m.p. 155-156° the mixed melting point of which, with diphenylacetaldehyde semicarbazone, gave no depression. The residue crystallized after the distillation; the crystals were pressed on a porous plate; m.p. 190-192°; it did not contain nitrogen, nor give a reaction for the aldehyde group. In view of the small amount of the substance, it was not investigated further; it is possible that this substance was the impurity which was present in the above obtained α-hydroxy-β,β-diphenylpropionitrile. Therefore, as the result of the hydrolysis of this nitrile, diphenylacetaldehyde was obtained.

Preparation of α-Amino-β,β-diphenylpropionitrile in Aqueous Ether Medium.

A solution of 23 g of diphenylacetaldehyde in 50 ml of ether and a solution of 8 g of NH_4Cl in 20 ml of water were placed into a bottle with a ground-in stopper. The bottle was placed in an ice bath, and a solution of 9 g of KCN in 25 ml of water was added dropwise to it; the bottle was then tightly stoppered, and the contents shaken on a shaker for 4 hours. The ether layer was separated, the aqueous solution extracted with ether, and the extracts dried with Na_2SO_4. In the remaining aqueous solution, nothing was found besides the inorganic substances. A stream of hydrogen chloride was passed through an ice cooled ether solution. After 10-15 minutes, a white crystalline residue of the hydrochloride precipitated. The residue was filtered and washed with ether; m.p. 202-203°. Weight 2 g which corresponded to 6.6 % of theory. After the separation of the hydrochloride from the ether solution saturated with hydrogen chloride, on standing a white crystalline substance, with m.p. 158-159° after recrystallization from water, came out. The substance did not contain halogen, gave a positive reaction for nitrogen, and a neutral reaction to litmus.

0.0882 g substance: 4.5 ml N_2 (18.5°, 758 mm). 0.0819 g substance : 17.5 ml CH_4 (17°, 742 mm). Found%: N 5.82; number of active hydrogens 2.07. $C_{15}H_{15}O_2$. Calculated % : N 5.80; the number of active hydrogen is 3 if it is considered that both nitrogens on NH_2 group reacted with the CH_3MgI; in the given case only one hydrogen of this group reacted.

An attempt was made to determine the neutral equivalent of this substance, but it could not be titrated in an alcoholic or an acetone solution. In order to effect a back titration, the substance was heated with an excess of 0.1 N alkali solution for 30 minutes. After the titration of the solution obtained with hydrochloric acid, a substance giving an acidic reaction was separated from the cooled solution, which melted at 146-150°. A mixed sample with the starting substance, with m.p. 158-159°, melted at 133-135°. On the basis of the results obtained, it could be considered that the substance obtained, with m.p. 158-159° is β,β-diphenyllactamide; even upon heating with a 0.1 N solution of the alkali for 30 mintues, it partly was hydrolyzed to β,β-diphenyllactic acid.

A second experiment was undertaken in order to obtain free diphenyllactic acid. In order to decrease the amount of unreacted diphenylacetaldehyde, the bottle with the ground-in stopper into which were placed, upon cooling, a solution of 20 g of NH_4Cl, in 35 ml of water, 65 g of diphenylacetaldehyde in 50 ml of ether, and 22 g of KCN in 30 ml of water, was shaken for 14 hours on the shaker; the ether layer was then separated, and combined with the extracts of the water layer. Upon passing hydrogen chloride through the dried and cooled ether solution, 8.5 g of a hydrochloride (~ 10%) came out. After its removal, a quantity of concentrated hydrochloric acid sufficient to produce a homogenous solution was added to the ether solution. The solution obtained was allowed to stand at room temperature for 7 days, and then water was added to it until two layers formed. The ether layer was separated, washed, and dried with Na_2SO_4. After the removal of the ether, a dark thick oil remained, which did not crystallize. It was boiled with water, and a white crystalline substance with m.p. 136-140° came from the water, which gave an acid reaction and contained, as shown by analysis, a nitrogen-containing substance as an impurity (% N 1.45). Diphenyllactic acid was isolated in pure form by going through the ammonium salt: 1 g of the substance with m.p. 136-140° was heated with an excess of a 6% ammonia solution on the water bath until the disappearance of the odor of ammonia. A white crystalline substance, in the form of starlike crystals characteristic for diphenyllactamide with m.p. 158-159°, formed in the cooled solution; a mixed melting point with authentic diphenyllactamide gave no depression. Weight of the amide, 0.17 g. The filtrate, after the removal of the amide, was acidified with hydrochloric acid to a weakly acidic reaction; needle-like crystals of diphenyllactic acid with m.p. 158-159° (from water) formed in the solution obtained on standing. A mixed sample with the amide with m.p. 158-159°, melted at 132-134°. Its silver salt was obtained by the action of $AgNO_3$ on the solution of ammonium diphenyllactate.

0.1009 g substance: 0.0309 g Ag; 0.0744 g substance: 3.3 ml NaOH (T 0.003279). Found %: Ag 30.62; E 242. $C_{15}H_{13}O_3Ag$. Calculated %: Ag 30.94. $C_{15}H_{14}O_3$; E 242.

Upon the hydrolysis of the nitrile, authentic synthesized diphenyllactic acid [18] (m.p. 158-159°) did not give a depression in melting point with the acid obtained.

Investigation of the Hydrochloride of α-Amino-β,β-diphenylpropionitrile

0.2243 g substance: 0.0244 g N_2 (according to Kjeldahl). 0.0726 g substance: 2.95 ml NaOH (T 0.003279). 0.0573 g substance: 15.2 ml CH_4 (16°, 761.7 mm). Found % : N 10.88; E 264; number of active hydrogens 3.12. $C_{15}H_{19}N_2Cl$. Calculated % : N 10.83; E 258.5; number of active hydrogens 3.

Hydrolysis of the Hydrochloride of α-Amino-β,β-diphenylpropionitrile

a) Upon heating the hydrochloride with 20% hydrochloric acid for 1 hour to boiling, in addition to the tarring products, nothing was obtained.

b) 1 g of the salt was dissolved in a mixture of 30 ml of ether and 50 ml of concentrated hydrochloric acid. The solution obtained was heated for 1 hour and 30 minutes on the water bath. In this case tarring also occurred.

c) 1 g of the salt was dissolved in a mixture of 30 ml of ether and 50 ml of concentrated hydrochloric acid. The solution obtained was allowed to stand for 10 days at room temperature, and then was evaporated on the water bath. The residual substance, washed with absolute ether, melted at 202-203°, and did not give a depression in melting point on being mixed with the starting salt. 0.75 g of the salt was recovered.

d) 1 g of the hydrochloride was heated on the water bath for 2 hours with 50 ml of a 25% solution of KOH. After cooling, an oil with an unpleasant odor floated on the surface of the solution; it was extracted with ether, and the extract obtained dried with Na_2SO_4. After the removal of the ether, 0.8 g of a liquid with an unpleasant odor, giving a neutral reaction, and forming a silver mirror by the action of an ammoniacal silver oxide solution, remained. With 2,4-dinitrophenylhydrazine, the substance obtained gave a 2,4-dinitrophenylhydrazone with m.p. 143-144° which did not give a depression in mixed melting point determination with authentic diphenylacetaldehyde 2,4-dinitrophenylhydrazone.

Preparation of α-Amino-β-hydroxy-β,β-diphenylpropionitrile in Aqueous Ether Medium

A solution of 12 g of NH_4Cl in 20 ml of water was added to 42 g of diphenylglycolic aldehyde dissolved in 80 ml of ether and placed in a bottle with a ground in stopper; the bottle was then placed in an ice bath, and 14 g of KCN in 25 ml of water was added slowly, dropwise to it. The bottle was stoppered and shaken for 4 hours on a shaker. At the end of the reaction, the ether solution was separated and dried with Na_2SO_4.

A small amount (0.16 g) of benzoic acid was isolated from the remaining aqueous solution. Upon passing hydrogen chloride through the ether solution obtained, 2 g of a crystalline substance (4%), readily soluble in alcohol, acetone, ethyl acetate, and water, came out. It did not dissolve with heating in chloroform or carbon tetrachloride. Washed with ether, it melted at 211-212°; a mixed sample with α-amino-β, β-diphenylpropionic acid hydrochloride with m.p. 202-203° melted at 188-189°.

0.1269 g substance: 0.1295 g N_2 (Kjeldahl). 0.1110 g substance: 3.56 ml NaOH (T 0.003279). 0.0572 g substance; 15.1 ml CH_4 (16° 761.7 mm). Found %: N 10.12; E 311; number of active hydrogen atoms 3.01. $C_{15}H_{15}ON_2Cl$. Calculated %: N 10.20; E 274.5; number of active hydrogen atoms 4 (counting both hydrogen atoms of the primary amino group).

In the second experiment on the synthesis of α-amino-β-hydroxy-β,β-diphenylpropionitrile conducted under the same conditions, a substance with m.p. 58-65°, a mixture of α-amino-β-hydroxy-β,β-diphenylpropionitrile and diphenylglyceric nitrile was obtained. A stream of hydrogen chloride was passed though part of the ether solution obtained during the reaction, and the hydrochloride of α-amino-β-hydroxy-β,β-diphenylpropionitrile with m.p. 211-213° was obtained. The rest of the ether solution was cooled to 0° and concentrated hydrochloric acid was added slowly to it to produce a homogeneous solution. After standing for four days, cold water was added until complete separation of the layers; the ether layer was removed, and dried with Na_2SO_4. After the removal of the ether, a yellow non-crystallizing oil remained. Part of it was heated with water, from which, on cooling, the starting substance with m.p. 58-63° precipitated. Another part of the oil was heated on the water bath with 6% ammonia solution until the complete disappearance of the ammonia odor. Upon the acidification of the filtered soltuion with hydrochloric acid, a small amount of a residue with m.p. 143-144° precipitated; after sublimation, it melted at 144-145° and did not give a depression with authentic diphenylacetic acid. The formation of the hydrochloride with m.p. 211-213° showed that the substance with m.p. 58-63° contained α-amino-β-hydroxy-β,β-diphenylpropionitrile, and the obtaining of diphenylacetic acid upon the hydrolysis of this substance, that it contained diphenylglyceric nitrile. The amount of the substance with m.p. 58-63° was small, 5 g, and could not be recrystallized.

SUMMARY

1. Under the conditions studied, α-amino-β-hydroxy-β,β-diphenylpropionitrile and α-amino-β,β-diphenylpropionitrile could not be obtained in good yields because of the difficulty of introducing an amino-group in the molecules of these nitriles and because of the instability of the compounds formed.

2. It was shown that diphenylglyceric nitrile was obtained when an attempt was made to synthesize α-amino-β-hydroxy-β,β-diphenylpropionitrile from diphenylglycolic aldehyde by the method of N. D. Zelinsky and G. L. Stadnikov in ether solution in the presence of 0.5 ml of water.

3. Upon the hydrolysis of diphenylglyceric nitrile in acidic medium, the diphenylglyceric acid formed dehydrated to form diphenylpyruvic acid, which is transformed on heating into diphenylacetic acid.

4. Upon the hydrolysis of diphenylglyceric nitrile in alkaline medium, in addition to diphenylpyruvic acid and diphenylacetic acid, the formation of benzhydrol occurred.

5. The reaction of diphenylacetaldehyde with KCN and NH_4Cl in ether solution in the presence of 0.5 ml of water led to the formation of diphenyllactonitrile. Upon its hydrolysis in acidic medium, the diphenyllactic acid formed decomposed with the formation of diphenylacetaldehyde.

6. In aqueous ether solution according to the method of N. D. Zelinsky and G. L. Stadnikov, the reaction of diphenylacetaldehyde with KCN and NH_4Cl proceeded in two directions: with the formation of α-amino-β-hydroxy-β,β-diphenylpropionitrile and diphenyllactonitrile. The yield of the aminonitrile was very small.

7. Upon the hydrolysis of the hydrochloride of the aminonitrile in acidic medium, in addition to tarring products, nothing else was obtained.

8. Upon the hydrolysis of the hydrochloride of the aminonitrile in alkaline medium, the cleavage of the nitrile occurred with the formation of diphenylacetaldehyde.

9. The reaction of an ether solution of diphenylglycolic aldehyde with an aqueous solution of KCN and NH_4Cl led to the formation of a mixture of diphenylglyceric nitrile and α-amino-β-hydroxy-β,β-diphenylpropionitrile.

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SYNTHESIS OF LEUCO BASES AND DYES OF THE TRIPHENYLMETHANE SERIES. III [1,2]

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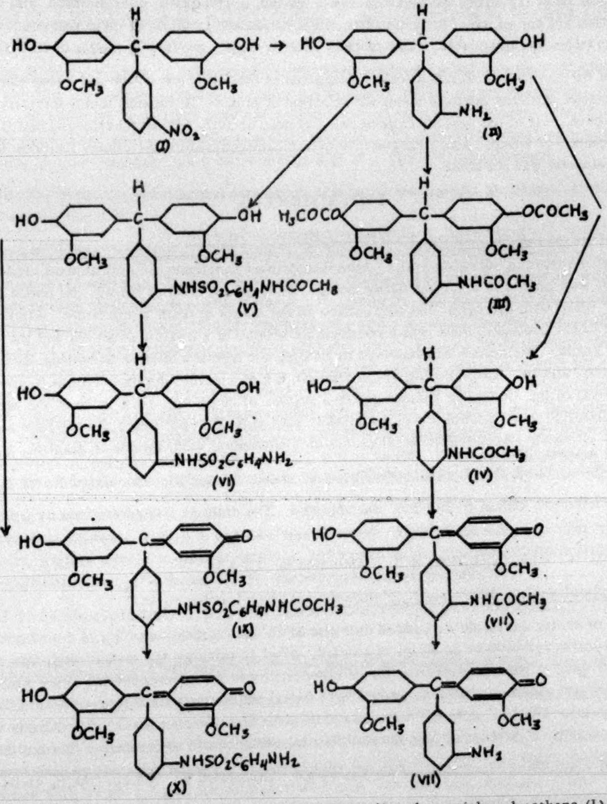
Continuing the investigation of compounds of the hydroxytriphenylmethane series with the aim of finding active anti-tuberculants among them, a series of substances was synthesized according to the following scheme:



The product of the reduction of 3-nitro-4',4''-dihydroxy-3',3''-dimethoxytriphenylmethane (I) [2] was used as the starting compound. The reduction was effected with hydrogen in the presence of a skeletonized nickel catalyst. 3-Amino-4',4''-dihydroxy-3',3''-dimethoxytriphenylmethane (II) was acetylated with acetic anhydride. Upon acetylation under various conditions, mono-, di-, and triacetyl derivatives were obtained from 3-amino-4',4''-dihydroxy-3',3''-dimethoxytriphenylmethane. By the condensation of compound (II) with p-acetylaminophenylsulfonyl chloride in pyridine, its acetylaminophenylsulfonamide derivative (V) was obtained. Saponification of the acetyl group was effected by heating with alkali (VI). The compound of the hydroxyfuchsone series was prepared by the oxidation of the leuco base with amyl nitrite in ethyl acetate which contained dry hydrogen chloride. The fuchsone hydrochloride obtained hydrolyzed quite readily in water; it gave a bright blue solution in alkalies (in a thin layer). In a thick layer, the alkaline solutions were colored red violet. Upon prolonged standing of the alkaline solutions of the hydroxyfuchsone derivatives in the air, they decolorized. A white residue was precipitated from the decolorized solution by the addition of sodium bisulfite or acetic acid, which however, started to darken upon drying in a desiccator or in the air. They could not be recrystallized, since they were partially transformed into hydroxyfuchsone derivatives. It is interesting to mention one outstanding property of the hydroxyfuchsone compounds obtained due to the presence of nitro, amino, acetylamino, sulfanilamido, and other substituents in position 3 of one of the phenyl nuclei of the hydroxyfuchsone molecule. Whereas hydroxyfuchsone compounds not containing these groups readily yield water-soluble bisulfite derivatives, often used for their preparation and isolation, the hydroxyfuchsines we obtained yield bisulfite derivatives only when they are heated with a large excess of sodium bisulfite, a considerable part of the substance not passing into solution. An analogous observation was found by Feldman and Prein [1] during the investigation of amino, acetylamino, sulfanilamido, and other rubrocols substituted in position 3 of one of the benzene rings. Purification and isolation of these compounds by means of bisulfite derivatives was impossible, while rubricol itself is readily purified by means of its bisulfite compound.

All of the compounds obtained were investigated in the laboratory of the All-Union Chemico-Pharmaceutical Scientific Research Institute under the direction of prof. G. N. Pershin, senior scientific coworker of O. O. Makeeva. All of the substances possessed a certain activity against tuberculosis bacilli in vitro and in the presence of serum. 3-Acetylaminophenylsulfonamidodihydroxydimethoxy fuchsone was the most interesting. However, its activity was not great.

EXPERIMENTAL

3-Amino-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane (II)

10 g of 3-nitro-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane, 150 ml alcohol, and 10 g of a skeletal nickel catalyst, were placed in a hydrogenation bottle. After the removal of the air, the bottle was connected with the apparatus, filled with hydrogen, and then shaken on the shaker at room temperature. After the cessation of the absorption of the hydrogen, there was a considerable residue of a mixture of amine and the catalyst on the bottom of the bottle. The amine was dissolved by heating the reaction mixture to boiling, and the solution was filtered from the catalyst. After cooling of the solution, 6 g of a white substance with m.p. 160-164° crystallized. After the removal of the alcohol in vacuum (up to a volume of 30-40 ml), 1.5 g more of the substance crystallized. After recrystallization from alcohol 7 g of a substance with m.p. 164-166° which did not increase any more, was obtained. The substance was insoluble in concentrated hydrochloric acid, soluble in alkalies, glacial acetic acid, acetone, ethyl acetate, and ether.

Found %: C 71.52, 71.77; H 6.13, 5.96; N 4.20, 3.97. $C_{21}H_{21}O_4N$. Calculated %: C 71.79; H 5.99; N 3.98.

A hydrochloride with m.p. 203-206° was obtained. The chlorine was determined by potentiometric titration.

Found %: Cl 9.20. $C_{21}H_{21}O_4N \cdot HCl$. Calculated %: Cl 9.16.

3-Acetylamino-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane (IV)

0.8 ml of acetic anhydride was added dropwise at 15° to a suspension of 2 g of 3-amino-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane in 50 ml of alcohol. After 10 minutes, the residue went into solution. After the solution had stood at room temperature for 30 minutes, it was poured into 200 ml of ice water. A white precipitate came out which was filtered, washed with water, and recrystallized from 30% alcohol. 1.9 g of a substance with m.p. 173-174°, 89% of theory, was obtained. The substance was readily soluble in alcohol and other organic solvents. A qualitative test showed that the substance did not contain a free amino group.

Found %: N 3.77, 3.67; $COCH_3$ 10.43. $C_{23}H_{23}O_5N$. Calculated %: N 3.56; $COCH_3$ 10.94.

3-Acetamino-4',4"-diacetoxy-3',3"-dimethoxytriphenylmethane (III)

2 g of 3-amino-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane and 10 ml of acetic anhydride were placed into a round-bottom flask equipped with ball condenser. The solution was heated for three hours at the boiling point. After cooling, it was poured on ice, the precipitate filtered, thoroughly washed with water, and dried. After recrystallization from 70% alcohol, 2.4 g of a substance with m.p. 162-163° was obtained. It was insoluble in water, alkalies, and benzene, and slightly soluble in alcohol and acetone. Yield, 90% of theory.

Found %: N 2.84, 2.78; $COCH_3$ 26.80. $C_{27}H_{27}O_7N$. Calculated %: N 2.93; $COCH_3$ 27.04.

The Diacetyl Derivative of 3-Amino-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane.

10 ml of glacial acetic acid and 15 ml of acetic anhydride were added to 3 g of 3-amino-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane. The solution was heated for 2 hours at 45-50° on the water bath, filtered, and poured dropwise on ice. A white flocculant precipitate separated. It was readily soluble in acetic acid, alcohol, acetone, and in dilute alcohol upon heating. Upon cooling the solution in aqueous alcohol, the substance came out in the form of an oil. It was slightly soluble in ether, but could be precipitated by it either from an alcohol or acetone solution. The substance was purified by dissolving in alcohol and pouring the alcoholic solution into water. The substance obtained (3 g) had an extended m.p. 75-90° and contained water of crystallization. A qualitative test with β-naphthol showed the absence of a free amino group.

Analysis of the compound obtained corresponded to the diacetyl derivative of 3-amino 4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane.

Found %: N 3.02, 2.98; CH_3CO 18.55; H_2O 3.5. $C_{25}H_{25}O_6N \cdot H_2O$. Calculated %: N 3.09; $COCH_3$ 18.96; H_2O 4.0.

Saponification of Acetyl Groups. A solution of 1 g of 3-acetylamino-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane in 5 ml of a 10% sodium hydroxide solution was heated to boiling on the screen for 1 hour, the solution was filtered, and carefully neutralized with hydrochloric acid to an acidic reaction. The excess hydrochloric acid was neutralized with a 10% sodium acetate solution. The precipitate obtained was washed and recrystallized from 10 ml of alcohol. 0.6 g of the amine with m.p. 162-163° was obtained.

The saponification of the di- and triacetyl derivatives also led to the starting 3-amino-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane (II).

3-Acetylaminophenylsulfonamido-4',4"-dihydroxy-3',3"-dimethoxy triphenylmethane (V).

2.7 g of 3-amino-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane and 20 ml of pyridine were introduced into a three-necked flask equipped with stirrer and thermometer, and placed into an ice bath. Then, 2.1 g of p-acetylaminophenylsulfonyl chloride was gradually added in small portions with stirring. After the addition of all of the acetylaminophenylsulfonyl chloride, which required 30-40 minutes, the stirring was continued for 30 minutes more at room temperature. The reaction mixture was then heated for 3 hours at 40-45° on the water bath. The solution was left to stand overnight. The next morning, it was filtered and poured dropwise with stirring into 2 liters of a 2% hydrochloric acid solution. A rose colored flocculant precipitate formed. It was washed with 2% hydrochloric acid until complete disappearance of the pyridine odor. 4 g of the dry substance with m.p. 245-246° was obtained. Yield, 95% of theory. It was slightly soluble in alcohol, aqueous alcohol, and other organic solvents; for this reason the purification was effected by many extractions with boiling alcohol.

3 g of a crystalline substance with m.p. 246-248° was obtained. Yield, 71% of theory. The substance was soluble in alkalies, slightly soluble in alcohol, acetone, and acetic acid. The analysis corresponded to 3-acetylaminophenylsulfonamido-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane.

Found %: C 63.34, 63.41; H 5.42, 5.13; N 5.22, 4.99; S 5.73; $COCH_3$ 7.80. $C_{29}H_{28}O_7N_2S$. Calculated %: C 63.68; H 5.11; N 5.11; S 5.84; $COCH_3$ 7.84.

3-Aminophenylsulfonamido-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane (VI).

A solution of 2 g of 3-acetylaminophenylsulfonamido-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane in 10 ml of a 10% sodium hydroxide solution was heated for 2 hours on the boiling water bath. The reaction mixture was filtered, cooled, and carefully neutralized with hydrochloric acid to an acidic reaction. The excess acid was neutralized by the addition of a saturated sodium acetate solution. The precipitated residue was filtered and washed with water; 1.5 g of the substance with m.p. 164-166° was obtained. Yield 55% of theory. The substance gave sharp depression in melting point when mixed with a sample of 3-amino-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane. It was insoluble in hydrochloric acid, benzene, and toluene, slightly soluble in alcohol acetone, and acetic acid, and readily soluble in alkalies.

Analysis of the substance corresponded to 3-aminophenylsulfonamido-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane.

Found %: C 64.15, 64.26; H 5.41, 5.18; N 5.46, 5.55; S 6.22, 6.11. $C_{27}H_{26}O_6N_2S$. Calculated %: C 64.05; H 5.53; N 5.53; S 6.32.

3-Acetylamino-4'-hydroxy-3',3"-dimethoxyfuchsone (VII).

A solution of 3 ml of freshly prepared amyl nitrite in 5 ml of ethyl acetate was added dropwise with stirring at 0-3° to a mixture of 6 g of 3-acetylamino-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane in 30 ml of ethyl acetate containing 15% of dry hydrogen chloride. The addition required 1 hour. The stirring was then continued for 3 hours more at 5-6°, and the mixture was left to stand overnight at the same temperature. The next morning, a residue had formed. It was filtered, washed with dry ethyl acetate, allowed to stand for 2-3 hours in ether, then filtered and dried in a vacuum desiccator. 6.2 g of the hydrochloride was obtained, which was a shiny violet crystalline substance similar to potassium permanganate in outward appearance. It melted at 125-127° with decomposition. According to analysis, the substance corresponded to 3-acetylamino-4'-hydroxy-3',3"-dimethoxyfuchsone containing one molecule of ether.

Found %: N 2.77, 2.88; Cl 7.42, 7.35; $C_4H_{10}O$ 14.92, 15.05. $C_{23}H_{22}O_5NCl \cdot C_4H_{10}O$. Calculated %: N 2.80; Cl 7.08; $C_4H_{10}O$ 14.77.

Upon washing the hydrochloride with distilled water, it lost chlorine and was transformed into the base which could not be recrystallized. Its solution in alcohol was yellow; evidently, it is completely dissociated. Upon treating the hydrochloride solution with a sodium acetate solution, it was colored blue. The substance obtained, upon washing with water, melted low and over a wide range. It was dissolved in acetic acid and poured into water; a red flocculant precipitate was obtained which gradually decomposed upon melting. The substance contained crystallization water. Analysis for the acetyl group showed that a partial saponification of the acetyl group, apparently, had occurred during the oxidation.

Found %: $COCH_3$ 9.44, 9.35; N 3.36, 3.41; H_2O 4.28. $C_{23}H_{21}O_5N \cdot H_2O$. Calculated %: $COCH_3$ 10.51; N 3.42; H_2O 4.40.

Upon drying in vacuum at 45-50°, the substance tarred. A crystalline substance could not be obtained from the hydrate. The substance was soluble in alcohol, acetone, acetic acid, and alkalies; it was insoluble in ether and benzene, and slightly soluble in ethyl acetate.

3-Amino-4'-hydroxy-3',3"-dimethoxyfuchsone (VIII)

10 ml of a 5% sodium hydroxide solution was added to 2 g of 3-acetylamino-4'-hydroxy-3',3"-dimethoxyfuchsone, and the solution was heated to boiling for 1 hour. The solution was filtered, made weakly acid to Congo, and a saturated sodium acetate solution was added until the acidic reaction disappeared. A brown-red amorphous residue precipitated; it could not be recrystallized; after two reprecipitations from an alkaline solution, 1.2 g of a substance was obtained; yield, 80% of theory. Its analysis corresponded to 3-amino-4'-hydroxy-3',3"-dimethoxyfuchsone containing 1 mole of water.

Found %: C 68.50, 68.35; H 5.58, 5.62; N 3.76, 3.86. $C_{21}H_{19}O_4N \cdot H_2O$. Calculated %: C 68.66; H 5.92; N 3.81.

It was not possible to determine the water of crystallization, since the substance decomposed partially upon drying in vacuum at 45-50°.

3-(p-Acetylaminophenylsulfonamido)-4'-hydroxy-3',3"-dimethoxyfuchsone (IX).

20 ml of ethyl acetate was added to 6 g of 3-acetylaminophenylsulfonamido-4',4"-dihydroxy-3',3"-dimethoxytriphenylmethane, and 30 ml of ethyl acetate containing 15% of gaseous HCl was added at 4-5°. Then a solution of 5 ml of freshly prepared amyl nitrite in 5 ml of dry ethyl acetate was added dropwise with stirring. The reaction mixture was stirred at this temperature for 3 hours more and was allowed to stand overnight at a temperature not greater than 10-12°. In the morning, the voluminous violet precipitate of the hydrochloride was filtered. The 6 g of the substance obtained was dissolved in 70 ml of dry acetone, the solution was filtered, and evaporated in vacuum at 20-25° to a residue of 10 ml. The acetone solution was then poured dropwise into 100 ml of dry ether. About 4 g of a dark violet residue with a metallic sheen precipitated. Some more of the hydrochloride, somewhat more impure, could be obtained from the solution after the removal of the solvents.

The analysis of the compound obtained corresponds to 3-acetytlaminophenylsulfonamido-4'-hydroxy-3',3"-dimethoxyfuchsone containing 1 mole of ether of crystallization.

Found %: Cl 5.22; $C_4H_{10}O$ 11.03, 10.95. $C_{29}H_{27}O_7N_2SCl \cdot C_4H_{10}O$. Calculated %: Cl 5.42; $C_4H_{10}O$ 11.28.

Upon heating the hydrochloride with a 10% solution of sodium acetate, or even better, with distilled water, the base was obtained, a dark red amorphous powder with a decomposition point of 182-185°. The substance did not contain water of crystallization. An analysis for the acetyl and sulfur corresponded to 3-(p-acetylaminophenylsulfonamido)-4'-hydroxy-3',3"-dimethoxyfuchsone.

Found %: N 4.88, 5.05; S 5.86, 5.94; $COCH_3$ 7.60, 7.30. $C_{29}H_{26}O_7N_2S$. Calculated %: N 4.94; S 5.84; $COCH_3$ 7.87.

3-(p-Aminophenylsulfonamido)-4'-hydroxy-3',3"-dimethoxyfuchsone (X).

20 ml of a 5% sodium hydroxide solution was added to 3 g of 3-(p-acetylaminophenylsulfonamido)-4'-hydroxy-3',3"-dimethoxyfuchsone, and the mixture was heated for 2 hours on the boiling water bath. The solution was filtered, and after cooling, carefully neutralized with hydrochloric acid to an acid reaction on Congo. The bright red amorphous residue which separated was filtered and washed several times with a small amount of distilled water. The substance, dried in a vacuum desiccator, over alkali did not have a sharp melting point; it melted low and over a wide range, gradually losing water during the melting.

The substance was soluble in acetone, alcohol, and acetic acid, very slightly soluble in ether, ethyl acetate, chloroform, benzene, and petroleum ether. After re-solution in alkali and reprecipitation with hydrochloric acid, and then with sodium acetate, the residue was thoroughly washed with water, dried in a desiccator, and analyzed. Its analysis corresponded to the calculated for 3-aminophenylsulfonamido-4'-hydroxy-3',3"-dimethoxyfuchsone containing 1 mole of water of crystallization.

Found %: N 5.45, 5.35; S 5.96, 6.10; H_2O 3.23. $C_{27}H_{24}O_6N_2S \cdot H_2O$. Calculated %: N 5.34; S 6.10; H_2O 3.43.

The substance was dissolved in acetone and precipitated from the solution with ether in the form of a residue with a green metallic sheen; it did not have a sharp melting point. Its analysis for sulfur corresponded to 3-aminophenylsulfonamido-4'-hydroxy-3',3"-dimethoxyfuchsone containing 1 mole of ether of crystallization.

Found %: S 5.50. $C_{27}H_{24}O_6N_2S \cdot C_4H_{10}O$. Calculated %: S 5.53.

SUMMARY

Nine leuco bases and dyes of the triphenylmethane series were prepared and characterized for the purpose of seeking substances active against tuberculosis bacilli.

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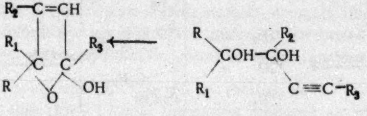
* See Consultants Bureau translation, p. 457.

INVESTIGATION OF HYDROXYDIHYDROFURANS

II. REACTION OF 2,4-DIPHENYL-5,5-DIMETHYL-2-HYDROXYDIHYDROFURAN-2,5 WITH ACETIC ANHYDRIDE

E. D. Venus-Danilova and A. N. Orlova

Substituted hydroxydihydrofurans of the general type (I) were first prepared by the catalytic action of sulfuric acid on pinacones of the acetylenic series (II) [1,2,3,4].



(I) (II)

An investigation of this reaction, conducted with various pinacones, enabled the authors to note a series of relations for the isomerization of these compounds and to show that the yields of the hydroxydihydrofurans depends, not only on the nature of the radicals in the pinacones, but also upon their mutual distribution in the molecule of the starting pinacone.

In certain cases, the hydroxydihydrofuran is the only product of the rearrangement of the pinacones [1,3]; in others, it is obtained in mixtures with isomeric ethyl γ-ketoalcohols [2], with acetylenic ketones [4,5,6], and sometimes are not even formed [7].

After a detailed study of the properties of these compounds, it was shown that they possess the property of giving oxonium compounds of varying stability [1,2,3,4], react with alcohols to form substances of the complete ketal type [3,8], give various bromination products with bromine [8], and are oxidized with great difficulty [9]. Upon catalytic hydrogenation, the hydroxyl group of the hydroxydihydrofurans is reduced first and then the double bond [9].

In the previous communication, the product of the reaction of 2,4-diphenyl-5,5-dimethyl-2-hydroxydihydrofuran-2,5 (I. R and $R_1 = CH_3$, R_2 and $R_3 = C_6H_5$) with acetic anhydride is reported.

A preliminary experiment conducted in 1914 with the substance when it was first obtained [1] for the purpose of showing a hydroxyl group in it, showed that a substance with an empirical formula $C_{20}H_{20}O_3$ was obtained with this reaction, which did not hydrolyze by the action of alkalies.

A more detailed study of this acetyl derivative, conducted at the present time, showed that this substance with m.p. 138-139° was not hydrolyzed by aqueous and alcoholic alkalies of various concentrations, and was recovered in the unchanged state upon acidification. It was also unchanged by the action of sulfuric acid of various concentrations and under various conditions.

The substance titrated bases, formed salts, was methylated with diazomethane, formed esters which could also be obtained by the action of methyl iodide on the silver salt. In addition, the amide could be obtained by means of the corresponding acid chloride.

Upon hydrogenation in the presence of platinum black, the substance with m.p. 138-139° added 2 atoms of hydrogen / mole, to form a new product which had acidic properties like the starting one.

On the basis of the above reaction, it must be considered that the substance with m.p. 138-139° is an unsaturated monobasic acid.

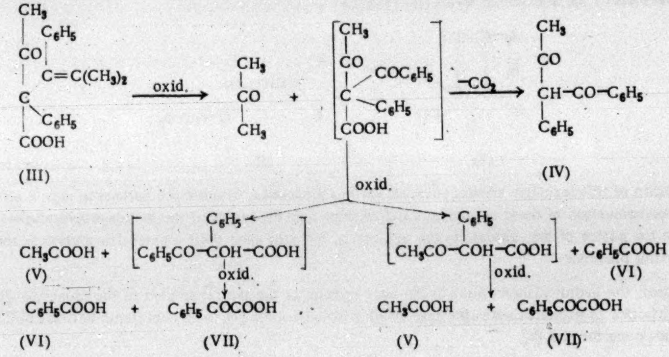
In order to determine the structure of the substance, it was subjected to the action of various oxidizing agents in acidic medium, for example: chromic anhydride, chromic mixture, but the product remained unchanged. Upon oxidation with hypoiodide, iodoform was detected; hypochlorite caused a strong tarring.

Upon oxidation by alkaline potassium permanganate solution, acetone and acetylbenzoylphenylmethane (IV) was detected in the neutral products. Carbon dioxide, acetic acid (V), benzoic acid (VI), and benzoylformic acid (VII) in the acidic (Scheme A).

The assumed oxidation products, diketo acid and the hydroxyketo acid (brackets in Scheme A), apparently, are rather unstable under the conditions of the reaction, decarboxylate, or are oxidized to the end products.

On the basis of all of the experimental data on the unsaturated monobasic acid with an empirical formula $C_{20}H_{20}O_3$ and m.p. 138-139° the structure oı disubstituted acetoacetic acid, phenyl-(1-phenyl)-isocrotylacetoacetic acid (III) must be assigned to it.

Scheme A



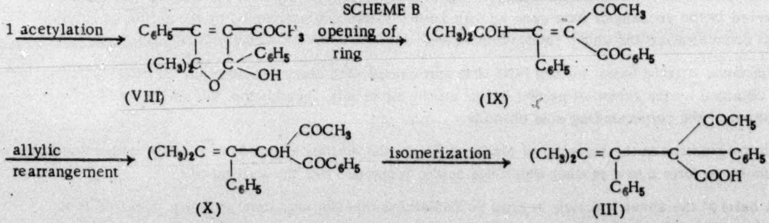
The stability of the acid obtained, in comparison to the simple acetoacetic acid, can evidently, be explained by the fact that electronegative radicals, phenyl and phenylisocrotyl, are found in the α-position to the carbonyl and carboxyl groups. It is known that homologs of acetoacetic acid [10,11,12,13] are more stable compounds.

The carbonyl group in the keto acids obtained could not be detected (the semicarbazone was not formed under the usual conditions) which can apparently be explained by steric hinderances.

An attempt to obtain this acid by the action of acetyl chloride on hydroxydihydrofuran was unsuccessful because of the strong tarring of the product.

In order to explain the formation of the substituted acetoacetic acid during the reaction of the hydroxydihydrofuran (I) (R and $R_1 = CH_3$; R_2 and $R_3 = C_6H_5$) with acetic anhydride, the following explanatory mechanism was proposed, which requires refinement and supplementation (Scheme B).

SCHEME B



The first stage of the reaction is the acetylation of the hydroxydihydrofuran to form the substituted 3-acetoxydihydrofuran (VIII) which can be compared to the acetylation of ethylenic hydrocarbons, first observed by I. Z. Kondakov [14] and later by other authors [15], with the formation of the unsaturated ketones. The second stage, the opening of the ring of the ring of the hydroxydihydrofuran is very clear, since under certain conditions, hydroxydihydrofurans can be transformed into unsaturated γ-ketoalcohols [2,8]. The allylic rearrangement of ethylenic alcohols is known extensively from the literature and is quite apparent for the given case. Finally, the last stage, the isomerization of the tertiary diketoalcohol (X) into the acid (III) is also possible, and an indirect proof is found in the literature on the many transformations of hydroxy carbonyl compounds and haloketones into acids [16,17,18,19].

EXPERIMENTAL

1. Action of Acetic Anhydride on 2,4-Diphenyl-5,5-dimethyl-2-hydroxydihydrofuran-2,5

The reaction was conducted under conditions previously reported [1] (by heating with 6 parts by weight of acetic anhydride for 40-45 minutes to slow boiling followed by pouring into an excess quantity of water.) The substance obtained was recrystallized from ether and was in the form of fine needles with m.p. 138-139°; yield, 85-88% of the theoretical based on the formula $C_{20}H_{20}O_3$. Elementary analysis and molecular weight determination confirmed this formula [1].

The substance was readily soluble in the common organic solvents, energetically reacted with methyl magnesium iodide, decolorized a chloroform solution of bromine, gradually decolorized an aqueous potassium permanganate solution, and did not react with semicarbazide, phenylhydrazine, and ferric chloride.

By the action of a 7% alcoholic potassium hydroxide solution (boiling for 5.5 hours), as well as a 10% alcoholic alkali by heating in a sealed tube (100°, 7 hours), the starting substance was recovered in quantitative yield upon acidification. The same results were obtained by the action of an excess of 50% aqueous alkali (100°, 3 hours).

The determination of the number of carboxyl groups by titration with alkali showed that the substance with m.p. 138-139° contained only one.

0.2094 g substance; 7.9 ml 0.1 N KOH solution. Found: 1.1 active hydrogen atoms.

The presence of one active hydrogen atom was confirmed by the determination of the number of hydroxyl groups by Terentyev's method.

0.0440 g substance: 3.5 ml CH_4 (10°, 760 mm). 0.0420 g substance: 3.5 ml CH_4 (19°, 763 mm). Found v_0 3.13, 3.22. % OH 5.3, 5.8. $C_{20}H_{19}O_2(OH)$. Calculated %: OH 5.5.

By the action of 7% and 12% sulfuric acid (100°, 5.5 hours) as well as 15% sulfuric acid (sealed tube, 6 hours, 15°), the substance was unchanged. A 12% aqueous alcoholic solution of sulfuric acid did not effect it (boiling, 3 hours).

2. Preparation of Salts of the Substance $C_{20}H_{20}O_3$

a) The ammonium salt was obtained by the saturation of 1.5 g of the substance in absolute ether with dry ammonia. The precipitated salt, after washing with absolute ether and drying, weighed 1.1 g, which corresponded to 95% of the theoretical.

0.1000 g substance: 3.31 ml 0.1 N solution H_2SO_4 (Kjeldahl). 0.1000 g substance: 3.24 ml 0.1 N solution H_2SO_4. Found %: N 4.50, 4.49. $C_{20}H_{23}O_3$. Calculated %: N 4.31.

b) The silver salt was obtained as a result of the exchange reaction between the ammonium salt and a saturated solution of silver nitrate. The precipitated white residue was washed with water and dried; yield 71.4% of the theoretical.

0.0999 g substance: 0.2133 g CO_2; 0.0440 g H_2O. 0.1014 g substance: 0.0262 g Ag. 0.1101 g substance: 0.0284 g Ag. Found %: C 58.17; H 4.89; Ag 25.84, 25.79. $C_{20}H_{19}O_3Ag$. Calculated %: C 57.83; H 4.58; Ag 26.02.

c) The barium salt was obtained by the exchange reaction of the ammonium salt with barium chloride. Yield, 46% of the theoretical.

0.1073 g substance: 0.0328 g $BaSO_4$. Found %: Ba 17.99. $C_{40}H_{38}O_6Ba$. Calculated %: Ba 18.28.

3. Preparation of Esters of the Substance $C_{20}H_{20}O_3$

a) Methylation with Diazomethane. 2 g of the substance with m.p. 138-139° was dissolved in 15 ml of absolute ether and poured into 175 ml of a 0.23% solution of diazomethane (theory, 0.29 g of diazomethane, i.e., 126 ml of the 0.23% ether solution). The reaction proceeded energetically with a rapid evolution of nitrogen. After 2 months, the ether was removed. The residue slowly crystallized. M.p. 64,65°. The substance did not contain nitrogen and did not react with methyl magnesium iodide.

0.1298 g substance: 0.3710 g CO_2; 0.0817 g H_2O. 0.0957 g substance: 0.2742 g CO_2; 0.0609 g H_2O. Found %: C 77.95, 78.14; H 6.99, 7.07. $C_{21}H_{22}O_3$. Calculated %: C 78.26; H 6.83 0.1101 g substance; 12.22 g C_6H_6: Δt 0.135°. Found M 334. $C_{21}H_{22}O_3$. Calculated M 322. 0.1763 g substance: 0.1134 g AgI. Found %; OCH_3 8.50. $C_{21}H_{22}O_3$. Calculated %: OCH_3 9.60.

Upon the hydrolysis of the substance obtained with a dilute aqueous potassium hydroxide solution using a slight amount of heat, and upon the subsequent acidification, a substance with m.p. 138-139° corresponding to $C_{20}H_{20}O_3$ precipitated.

b) Methylation Starting with the Silver Salt. A small amount of methyl alcohol and 1 g of methyl iodide were added to 0.5 g of the silver salt of $C_{20}H_{20}O_3$. The mixture was heated for 15 hours at 65°. After 24 hours, an ether extraction was made which gave an oily substance crystallizing after several days. M.P. 64-65°. This substance was found to be identical (mixed melting point) to the methyl ester obtained with diazomethane.

4. Preparation of the Amide of the Substance $C_{20}H_{20}O_3$

The amide was obtained by the usual method by means of the acid chloride [20]. The thick yellowish mass of the acid chloride was dissolved in absolute ether and saturated with dry ammonia; the precipitated white mass was washed with petroleum ether and recrystallized from a mixture of ether and petroleum ether. M.p. 92-93.5°: Yield 65% of the theoretical.

0.1030 g substance: 0.2963 g CO_2; 0.0664 g H_2O. 0.1332 g substance: 5.7 ml N_2 (20°, 762 mm). 0.1269 g substance: 5.1 ml N_2 (17°, 768 mm). Found %: C 78.46; H 7.16; N 4.88, 4.69. $C_{20}H_{21}O_2N$ Calculated %: C 78.18; H 6.84; N 4.56. 0.1468 g substance; 13.62 g C_6H_6: Δt 0.18°. Found M 300. $C_{20}H_{21}O_2N$. Calculated M 307.

5. Hydrogenation of the Substance $C_{20}H_{20}O_3$

The reduction was effected with platinum black until two atoms of hydrogen had added per mole of the starting substance.

1 g of the substance with m.p. 138-139°, dissolved in 160 ml of ethyl alcohol, in the presence of 0.5 g of platinum black, absorbed 79 ml of hydrogen (15°, 751.5 mm) which indicated the presence of one ethylene bond in the molecule. The reaction proceeded slowly, and after the absorption of 79 ml of hydrogen, practically stopped.

After the removal of the alcohol, the caramel-like mass crystallized upon the addition of petroleum ether. After thorough washing with petroleum ether and recrystallization from ethyl ether, 1.6 g of a product with m.p. 128-129° was obtained as a result of the hydrogenation of 4 g of the substance with m.p. 138-139° (5 experiments). Yield 40% of the theoretical. The substance gave a depression in melting point with the starting material, was poorly soluble in glacial acetic acid, readily in ether and benzene, and did not decolorize an aqueous potassium permanganate solution or a chloroform solution of bromine, contained an active hydrogen, and showed acidic properties; it dissolved in aqueous alkalies and sodium carbonate solution, and was recovered upon acidification. The carbonyl group could not be detected.

0.1186 g substance: 0.3374 g CO_2; 0.0716 g H_2O. 0.0871 g substance: 0.2466 g CO_2; 0.0556 g H_2O. Found %: C77.63, 77.26; H 6.84, 7.14; $C_{20}H_{22}O_3$. Calculated %: C 77.40; H 7.09. 0.1497 g substance; 11.80 g C_6H_6: Δt 0.19°. Found M332. $C_{20}H_{22}O_3$. Calculated M 310. 0.0338 g substance: 2.7 ml CH_4 (19°, 746.5 mm). Found v_0 CH_4 2.46 ml; %: OH 5.52. $C_{20}H_{21}O_2(OH)$. Calculated v_0 2.43 ml; %: OH 5.48. 0.1400 g substance: 5.14 ml 0.1 N KOH solution. Found one carboxyl group.

In view of the small amount of the substance it was not studied further.

6. Oxidation of the Substance $C_{20}H_{20}O_3$

a) Oxidation with alkali hypochloride did not lead to satisfactory results. A strong tarring occurred. Chloroform could not be detected, only a small amount of benzoic acid could be isolated, which was characterized by melting point (mixed melting point) and analysis of the silver salt. Found %: Ag 46.91. Calculated %: Ag 47.16.

b) Oxidation with Hypoiodite. The corresponding quantity of finely pulverized iodine was added to a solution of the substance in alkali. Upon heating, a cloudiness appeared, and the odor of iodoform could be detected.

c) Oxidation with Chromic Anhydride. A solution of 2.16 g of chromic anhydride in 22 ml of water (10 moles of the anhydride for 3 moles of substance) was added with efficient stirring to 2 g of the substance with m.p. 138-139° and 8.3 g of potassium sulfate ground into a powder. No change in color occurred, and the substance was recovered unchanged even when the reaction mixture was heated to boiling for 6 hours.

d) Oxidation with Chromic Mixture. The calculated amount of chromic mixture (1.63 g of potassium dichromate, 13.6 g of sulfuric acid, d 1.83, diluted with 6 volumes of water [21]) was used for 1 g of the substance.

The chromic mixture was added in 2 parts with stirring and heating for 5 hours on the boiling water bath. No change in color occurred. After the usual processing of the reaction mixture, the starting substance with m.p. 138-139° was isolated in quantitative yield.

e) Oxidation with Potassium Permanganate. Five experiments were conducted on the oxidation with changes in the reaction conditions. The best results were obtained with the following conditions: 100 ml of a 2% potassium permanganate solution and 7 ml of a 10% potassium hydroxide solution, for the conversion of the substance into a water-soluble salt, was added to 2 g of the substance. Decolorization started very rapidly and the reaction proceeded with the slight evolution of heat. The remaining 1.61 g of potassium permanganate was added in dry form in 3 portions over 1.5 hours. During the oxidation a frothing of the liquid and evolution of carbon dioxide gas occurred which was absorbed by baryta water by passing air, minus carbon dioxide, through the apparatus. After 3 hours, a complete decolorization of the solution and separation of the manganese dioxide had occurred. 10 ml of a 5% potassium hydroxide solution was then added to the reaction mass in order to combine with the acids formed during the oxidation. After 15-20 minutes, the possible excess of free alkali was neutralized with the passage of carbon dioxide. The manganese dioxide was filtered, washed with water and ether, and the neutral and acidic products were subjected to investigation.

The neutral products were distilled at a slight vacuum at 55-60° on the water bath, in small portions, into a solution of p-nitrophenylhydrazine; an orange precipitate formed at once. From the first portion, the residue melted at 142-145° (Melting point of acetone p-nitrophenylhydrazone, 148°); in subsequent portions, the melting point decreased to 114-116°. Evidently, the acetone, detected by the iodoform and sodium nitroprusside test, was mixed with neutral products volatile in steam which also reacted readily with p-nitrophenylhydrazine.

Upon increasing the heating temperature, a substance with a pleasant floral odor with an extended melting point 91-93° was extracted with ether from the 3rd portion of the distillate.

0.0929 g substance: 0.2739 g CO_2; 0.0518 g H_2O. Found %: C 80.41; H 6.19. $C_{16}H_{14}O_2$. Calculated %: C 80.67; H 5.88.

The substance was volatile, very readily soluble in all organic solvents, did not decolorize in the cold aqueous potassium permanganate or chloroform bromine solutions, did not color fuchsine sulfurous acid solution, did not react with Fehling's solution and ammoniacal silver oxide solution; it reacted with methyl magnesium iodide and ferric chloride; it also gave the characterisitic reaction for enols with copper acetate. With an aqueous solution of p-nitrophenylhydrazine, it rapidly formed an orange precipitate with m.p. 137-138° giving a depression in melting point with authentic acetone p-nitrophenylhydrazone (the mixture melted at 119-125°.):

0.0900 g substance: 9.0 ml N_2 (14°, 769 mm). 0.0898 g substance: 9.5 ml N_2 (18°, 757.5 mm). Found %: N 11.83, 12.12. $C_{22}H_{17}O_2N_3$. Calculated %: N 11.83.

On the basis of the above properties and elementary analysis, the neutral substance with m.p. 91-93° must be considered to be a β-diketone, acetylbenzoylphenylmethane (1,2-diphenylbutan dione-1,3) (IV), while the product of its reaction with p-nitrophenylhydrazine with m.p. 139-139°, the pyrazolone corresponding to it.

Among the acidic oxidation products, isolated in the usual manner, were detected: benzoylformic acid, but its reaction with phenylhydrazine (melting point of the phenylhydrazone, 153°), a small amount of the starting substance, and benzoic acid purified by sublimation and not giving a depression in melting point with authentic benzoic acid.

The steam-volatile acids were distilled by boiling the solution and were collected in separate portions. In the last portions, acetic acid distilled and was characterized by analysis of the silver salt. Found %: Ag 64.55; Calculated %: Ag 64.65.

Therefore, the products of the oxidation of the substance with m.p. 138-139° supported the proposed structure as the disubstituted acetoacetic acid.

It must be mentioned that an excess of the oxidant did not increase the yield of the oxidation products, but, conversely, decreased the yield of the diketone from 33-35% to 15-18%. It also must be mentioned, if alkali was not added at the start of the oxidation, then it occurred slowly, and 10-13% of the starting product was recovered. If immediately after the oxidation the free alkali was not neutralized with carbon dioxide, and the neutral products were not distilled at once, then a small amount of the volatile mesityl oxide was mixed with the acetone and the β-diketone, which was formed by the condensation of acetone in the presence of alkali. Contamination with mesityl oxide can explain the wide and low melting point of the acetone phenylhydrazone which was mixed with mesityl oxide pyrazoline (m.p. 128-129°), as well as the decreased yields of acetone.

The presence of mesityl oxide in the alkaline solution was confirmed by the preparation and analysis of the corresponding semicarbazone (m.p. 163-164°), and pyrazoline (m.p. 128-129°). An artificial mixture prepared from equal amounts of authentic acetone p-nitrophenylhydrazone and mesityl oxide pyrazoline, melted at 113-118°.

SUMMARY

1. Phenyl-(1-phenyl)-isocrotylacetoacetic acid is formed by the reaction of 2,4-diphenyl-5,5-dimethyl-2-hydroxydihydrofuran-2,5 with acetic anhydride; its salts, esters and amide were prepared.

2. The structure of the acid obtained was proved by the products of its oxidation: acetone, 1,2-diphenylbutandione -1,3, benzoylformic, benzoic, and acetic acids, as well as its reduction to the corresponding phenyl-(1-phenyl)-isobutylacetoacetic acid.

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SYNTHESIS OF ISONICOTINIC HYDRAZIDE DERIVATIVES

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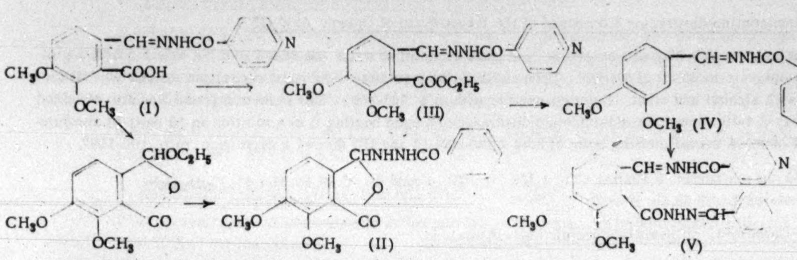
In a paper by the authors with G. N. Pershin, O.O. Makeev, E. S. Nikitskaya, A. D. Yanina, and A. I. Yakovleva [1], a new group of compounds possessing antitubercular activity in vitro and good therapeutic action for experimental tuberculosis in animals was reported. One of these preparations, called Phtivazide by the authors, showed good clinical results for tubercular therapy and was recommended for extensive application. In this investigation it was established that aromatic isonicotinoyl hydrazones exceeded isonicotinic hydrazide, which was also investigated by the authors and was studied in detail and recommended by a series of foreign authors under the names of Nydrazid,, Rimifon, Neoteben, etc., in antitubercular activity and tolerance. Several months after the publication of the authors' paper, the German investigator Domagk [2] came to the same conclusion of the superiority of isonicotinoylhydrazones over isonicotinic hydrazide.

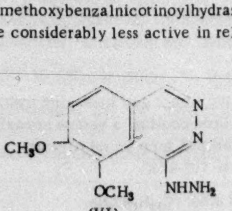
Continuing the investigation on the synthesis of compounds containing an isonicotinic acid residue and the group $=\overset{|}{C}-NH-N=\overset{|}{C}-$, which is peculiar to a series of substances posesing high tuberculostatic activity (thiosemicarbazones, derivatives of aminothiazoles, amidrazones, phthalazones), it was considered of interest to prepare substances in which this group is repeated. For this purpose, 2-carboxy-3,4-dimethoxybenzalisonicotinoylhydrazone (I) was prepared, transformed by means of the ester (III) into the hydrazide of the acid (IV), and the latter condensed with salicylaldehyde into hydrazone (V):



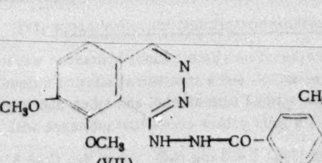
It must be mentioned that, upon heating opianic acid isonicotinoylhydrazone in alcoholic solution, it is transformed into a derivative of pseudo-opianic acid (II) which was also obtained from the pseudo ester of opianic acid and isonicontinoylhydrazide. Its pseudo structure was confirmed by its insolubility in sodium bicarbonate solution.

Compounds were also synthesized where the group with the two nitrogen atoms was separated by one carbon atom, 4-isonicotinoylhadrazino-5,6-dimethoxyphthalazine and the corresponding nicotinic acid derivatives.

Upon the study of the inhibitory action on the development of tuberculosis bacillus in vitro, it was found that the introduction of a second $=C-NH-N=\overset{|}{C}-$ group into the aromatic isonicotinoylhydrazones led to a considerable decrease in the antitubercular activity. For comparison, derivatives of nicotinic acid were also prepared, 2-carboxy-3,4-dimethoxybenzalnicotinoylhydrazone and 5,6-dimethoxy-4-(nicotinoylhydrazino)-phthalazine. These compounds were considerably less active in relation to the tuberculosis bacillus than the corresponding isonicotinic acid derivatives.



(VI)



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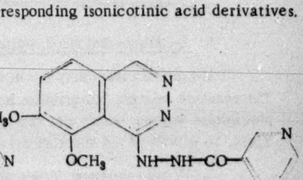

(VIII)

EXPERIMENTAL

1. 2-Carboxy-3,4-dimethoxybenzalisonicotinoylhydrazone (I)

A hot solution of 1.37 g of isonicotinic hydrazide was added with stirring to a hot (90°) solution of 2.1 g of opianic acid in 40 ml of water; the solution was colored yellow-green by this addition, and a voluminous precipitation of light yellow crystals began. On cooling, they were filtered, washed with water, alcohol, and ether. Light yellow needles with m.p. 205-206°. It contained 1 mole of water of crystallization which was given off at 160°. Yield, 3.21 g (98% of the theoretical).

2.918 mg substance: 6.2321 mg CO_2 and 1.179 mg H_2O. Found %: C 58.27; H 4.52. $C_{16}H_{15}O_5N_3$. Calculated %: C 58.35; H 4.55.

Salts:

$C_{16}H_{14}O_5N_3Na$ - colorless crystals (from 4 parts of water). M.P. 239-240°.

$C_{16}H_{15}O_5N_3 \cdot NH(CH_2CH_2OH)_2$ -- colorless crystals (from 50 parts of alcohol). M.p. 196-197°, readily soluble in water.

$C_{16}H_{15}O_5N_3 \cdot NH(C_2H_5)_2$ -- colorless crystals (from two parts of alcohol). M.p. 176-177°, very readily soluble in water.

Aqueous solutions of these salts gradually clouded on standing forming a precipitate of these salts.

2. Isonicontinoylhydrazine Compound of the Pseudo-Form of Opianic Acid (II)

A hot solution of 1.37 g of isonicotinic hydrazide in 10 ml of water was added to a hot solution of 2.1 g of ethyl pseudo-opianate in 20 ml of alcohol. Upon cooling, the precipitated colorless crystalline residue was filtered and washed with alcohol and ether. Colorless needles with m.p. 207-208°. This same compound was also obtained from 2-carboxy-3,4-dimethoxybenzalisonicotinoylhydrazone (I) upon heating it in a solution in 10 parts of absolute alcohol for 1 hour. A mixed melting point of both substances (I) and (II) showed a depression; m.p. 190-198°.

2.770 mg substance: 5.932 mg CO_2; 1.108 mg H_2O. Found %: C 58.44; H 4.47. $C_{16}H_{15}O_5N_3$. Calculated %: C 58.35; H 4.55.

3. 2-Carboxy-3,4-dimethoxybenzalnicotinoylhydrazone.

It was prepared under the same conditions as the previous preparation. Colorless prismatic platelets. It contained 1 mole of water of crystallization which was lost at 150°. M.p. 214-216°. Yield 97% of the theoretical.

3.528 mg substance: 7.532 mg CO_2; 1.451 mg H_2O. 2.795 mg substance: 0.326 ml N_2 (23°, 738.0 mm). Found %: C 58.26; H 4.60; N 13.06. $C_{16}H_{15}O_5N_3$. Calculated %: C 58.35; H 4.55; 12.76.

4. (2-Carbethoxy-3,4-dimethoxybenzal)isonicotinoylhydrazone (III)

3.2 g of acid (I) and 50 ml of ethyl alcohol, saturated with hydrogen chloride, was heated for 3 hours on the water bath. Upon cooling, the yellow crystalline precipitate was washed with alcohol and ether. Yield, 2.5 g of the hydrochloride from which the base was separated by treatment with sodium bicarbonate. It was recrystallized from alcohol. Colorless needles with m.p. 213-214°.

5.190 mg substance: 0.556 ml N_2 (22°; 733 mm). Found %: N 11.85. $C_{18}H_{19}O_5N_3$. Calculated %: N 11.76.

5. 2-Carbohydrazido-3,4-dimethoxybenzalisonicotinoylhydrazone (IV)

1.8 g of (2-carbethoxy-3,4-dimethoxybenzal)isonicotinoylhydrazone was treated with 2 g of hydrazine hydrate. The reaction mixture temperature rose to 70°, and a transparent solution formed. Upon cooling, a yellow crystalline precipitate formed, which was filtered, washed with alcohol and ether, and recrystallized from 30 ml of water. Yield, 15 g (87% of the theoretical) of a light yellow crystalline substance with m.p. 152-153°.

3.457 mg substance: 7.058 mg CO_2; 1.433 mg H_2O. Found %: C 55.81; H 4.64. $C_{16}H_{17}O_4N_5$. Calculated %: C 55.97; H 4.92.

6. o-Hydroxybenzal Derivative of(2-Carbohydrazido-3,4-dimethoxybenzal)isonicotinoylhydrazone (V)

A hot solution of 0.6 g of salicylaldehyde in 10 ml of alcohol was added with shaking to a hot solution of 1.5 g of the previous compound. Upon cooling, the precipitate which formed, was filtered, washed with alcohol and ether, and recrystallized from 30 ml of water. Colorless long platelets. M.p. 210-211. Yield 1.9 g.

3.549 mg substance: 8.005 mg CO_2; 1.462 mg H_2O. 3.632 mg substance: 0.518 ml N_2 (26°; 738 mm). Found %: C 61.55; H 5.48; N 15.80. $C_{23}H_{22}O_5N_5$. Calculated %: C 61.45; H 5.12; N 15.59.

7. 4-Hydrazino-5,6-dimethoxyphthalazine (VI)

A mixture of 10 g of 4-chloropiazine [3] and 20 g of hydrazine hydrate was heated on the water bath to 30°. A reaction started, the temperature of the solution rose spontaneously, and the solution turned transparent. Upon cooling yellow crystals of 4-hydrazino-5,6-dimethoxyphthalazine precipitated which were filtered and dried. M.p. 75-76°; they are readily soluble in water and alcohol. Yield 8 g. The base was converted to the hydrochloride by adding 5 ml of concentrated hydrochloric acid to its solution in 20 ml of alcohol. The colorless crystals of the hydrochloride which formed were filtered, washed with alcohol and ether, and recrystallized from 15 ml of water. Colorless crystals with m.p. 164-165°.

4.040 mg substance: 6.910 mg CO_2; 1.760 mg H_2O. 3.512 mg substance: 0.652 ml N_2 (21°, 744.0 mm). 19.219 mg substance: 3.71 ml $AgNO_3$. Found %: C 46.57; H 5.18; N 22.30; Cl 13.69. $C_{10}H_{12}O_2N_4 \cdot HCl$. Calculated %: C 46.78; H 5.07; N 21.83; Cl 13.84.

8. 5,6-Dimethoxy-4(isonicotinoylhydrazino)-phthalazine (VII)

A mixture of 2.25 g of chloropiazine, 1.37 g of isonicotinic hydrazide, and 20 ml of alcohol was heated for 1 hour on the water bath. Upon cooling a colorless, crystalline precipitate formed, which was filtered, washed with alcohol and ether, and recrystallized from 50 ml of alcohol. Yield 3 g (90% of the theoretical). Colorless needles with m.p. 234-235° (with decomposition).

3.640 mg substance: 7.858 mg CO_2; 1.450 Mg H_2O. Found %: C 58.91; H 4.60. $C_{16}H_{14}O_3N_5$. Calculated %: C 59.07; H 4.61

9. 5,6-Dimethoxy-4(nicotinoylhydrazino)-phthalazine (VIII)

It was prepared in the same manner as the previous preparation. Colorless crystals with m.p. 207-208°. Yield 90% of the theoretical.

3.528 mg substance: 7.600 mg CO_2; 1.380 mg H_2O. Found %: C 58.79; H 4.70. $C_{16}H_{15}O_3N_5$. Calculated %: C 59.07; H 4.61.

SUMMARY

A series of new compounds was prepared in order to investigate antitubercular activity, which were simultaneously, derivatives of isonicotinic or nicotinic hydrazide and opianic acid. It was shown that the isonicotinoylhydrazone obtained from opianic acid, was easily transformed into the isonicotinoylhydrazino compound of phthalide structure which was obtained directly from the ester of opianic acid.

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THIAZOLIDINE -4- CARBOXYLIC ACID AND ITS DERIVATIVES
V. STUDY OF S(2-PHENYL-5-OXAZOLONEMETHYLENE-4)-N-ACETYLCYSTEINE AND ITS ANALOGS

I. T. Strukov

By a study of the mechanism of the formation of 4-alkylidene-2-phenyl-5-oxazolones, it was established that the reaction occurs in two stages: first, 2-phenyl-5-oxazolone is formed from hippuric acid and acetic anhydride, and then it reacts with aldehydes or ketones, whereby the presence of water-removing substance does not appear to be necessary for the second stage of the reaction [1]. Therefore, upon the transition of hippuric acid into 2-phenyl-5-oxazolone, the reactivity of the hydrogen atoms is greatly increased.

The transformation of the more complex α-acylamino acids into saturated oxazolones is also accompanied by an increase in the activity of the hydrogen atoms in position 4, as well as on its neighboring carbon atoms. This property of saturated oxazolones is expressed by their ability to be transformed into unsaturated compounds. For example, unsaturated oxazolones [2] can be obtained from N(α-haloidacyl) amino acids, 4-methoxymethylene-2-benzyl-5-oxazolone can be synthesized from the dimethylacetal of formylphenaceturic acid, whereby the simultaneous cleavage of one molecule of methyl alcohols occurs during the cyclization of the oxazolone ring [3], and the rearrangement of benzylpenicillonic acid into benzylpenicillenic acid [4].

The last reaction was unexpected and very interesting, since the preparation of benzylpenicillin was being attempted by the action of water-removing substances on benzylpenicillonic acid.

Therefore, the cyclization of the oxazolone ring leads to a new distribution of energy of the chemical affinity to the CH_2 group (in 2-phenyl-5-oxazolone) and to the CH group (in other saturated oxazolones). The hydrogen is found to be so weakly bound that it readily leaves the carbon atom. The conjugated system of double bonds formed in this manner stabilizes the oxazolone ring to an apparent extent, which can be seen upon comparison of the stability of the saturated and unsaturated oxazolone rings [5].

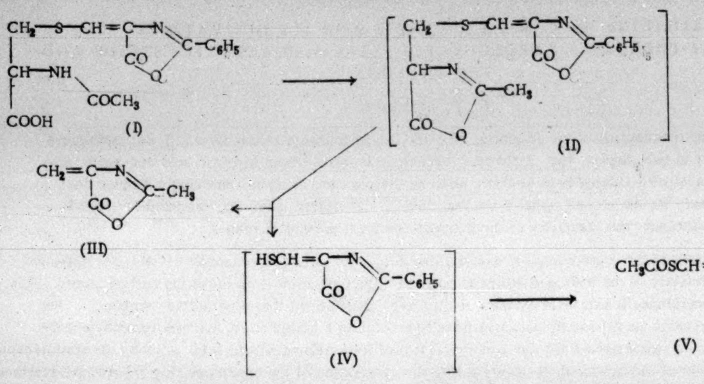
The above property of oxazolones was found also to be applicable to derivatives of S(2-phenyl-5-oxazolonemethylene-4)-N-acetylcysteine and its analogs [6], the study of which is the subject of the present investigation.

Upon heating S(2-phenyl-5-oxazolonemethylene-4)-N-acetylcysteine (I) with acetic anhydride, a bright yellow crystalline substance with m.p. 174-176° was obtained. It could be supposed that a compound with two oxazolone rings (II) had formed; this was not confirmed by analysis. This type of compound is formed by the reaction of acetic anhydride with S(2-phenyl-5-oxazolonemethylene-4)-N-acetylpenicillamine. Therefore, it follows that the right part of the molecule of both compounds participated in the reaction, which was 4-mercaptomethylene-2-phenyl-5-oxazolone. It can be expected that the hypothetical product (II) with two oxazolone rings, formed from S(2-phenyl-5-oxazolonemethylene-4)-N-acetylcysteine, easily decomposes into two unsaturated oxazolones: 4-methylene-2-methyl-5-oxazolone (III) and 4-mercaptomethylene-2-phenyl-5-oxazolone (IV). The bright yellow compound obtained with m.p. 174-176° could be considered the product of the reaction of 4-mercaptomethylene-2-phenyl-5-oxazolone with the excess of acetic anhydride. This compound could have been 4-acetomercaptomethylene-2-phenyl-5-oxazolone (V) since the analytical results upheld this possibility.

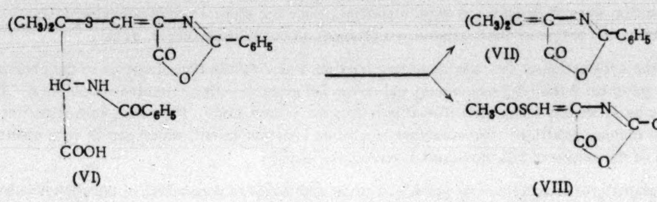
Actually, 4-mercaptomethylene-2-phenyl-5-oxazolone, prepared by A. Ya. Berlin and V. I. Maimind's [7] method, was easily transformed into 4-acetothiomethylene-2-phenyl-5-oxazolone with m.p. 174-176° by heating with acetic anhydride.

The mechanism of this reaction is shown by the following scheme: (see top of next page)

In order to establish the reaction mechanism beyond doubt, N-benzoylpenicillamine was prepared. By condensing N-benzoylpenicillamine with 4-ethoxymethylene-2-phenyl-5-oxazolone in pyridine, we prepared S(2-phenyl-5-oxazolonemethylene-4)-Nbenzoylpenicillamine (VI), which, upon heating with acetic anhydride gave 4-isopropylidene-



2-phenyl-5-oxazolone (VII) and 4-acetothiomethylene-2-phenyl-5-oxazolone (VIII).



For the identification of the reaction product (VII), 4-isopropylidene-2-phenyl-5-oxazolone [8] was prepared. Analysis, crystal form, and absence of a depression in melting point did not leave any doubt that the second product of the reaction was 4-isopropylidene-2-phenyl-5-oxazolone (VII).

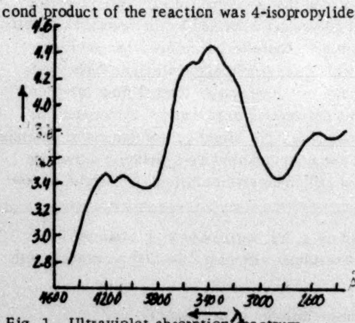


Fig. 1. Ultraviolet absorption spectrum of 4-acetothiomethylene-2-phenyl-5-oxazolone obtained from S(2-phenyl-5-oxazolonemethylene-4)-N-acetylcysteine.

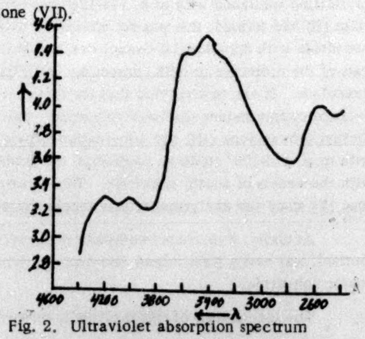


Fig. 2. Ultraviolet absorption spectrum of 4-acetothiomethylene-2-phenyl-5-oxazolone obtained from 4-mercaptomethylene-2-phenyl-5-oxazolone.

In order to prove the identity of 4-acetothiomethylene-2-phenyl-5-oxazolone obtained from various compounds, their ultra-violet absorption spectra were determined in the physico-chemical laboratory of the All-Union Scientific Chemico-Pharmaceutical Research Institute by Yu. N. Sheinker and B. M. Golovner. The 4-acetothiomethylene-2-phenyl-5-oxazolones obtained from S(2-phenyl-5-oxazolonemethylene-4)-N-acetylcysteine (I) (Fig. 1) and from 4-mercaptomethylene-2-phenyl-5-oxazolone (Fig. 2) were compared. Their absorption spectra were found to be identical containing intense bands with $\lambda_{max.}$ = 3600 A and 3450 A.

As was previously shown [9], there is a characteristic absorption band with $\lambda_{max.}$ = 3600 A in the absorption spectra of S-methylene substituted 2-phenyl-5-oxazolones.

The presence of the band $\lambda_{max.}$ = 3600 A in the spectrum of 4-acetothiomethylene-2-phenyl-5-oxazolone serves as a supplementary proof of its structure.

As for the band $\lambda_{max.}$ = 3450 A, it apparently can be viewed as being the result of the effect of the acetyl group directly attached with a sulfur atom.

The presence of two other bands of small intensity with $\lambda_{max.}$ = 4050 A and 4200 A can be assigned to a small impurity of bis-(2-phenyl-5-oxazolonemethylene-4)sulfide. Actually, upon purifying 4-acetothiomethylene-2-phenyl-5-oxazolone, a small amount of a substance with m.p. 233-234° (with decomposition), could be isolated, and it was shown that it was bis(2-phenyl-5-oxazolonemethylene-4)sulfide. The latter was prepared by the condensation of 4-ethoxymethylene-2-phenyl-5-oxazolone with 4-mercaptomethylene-2-phenyl-5-oxazolone.

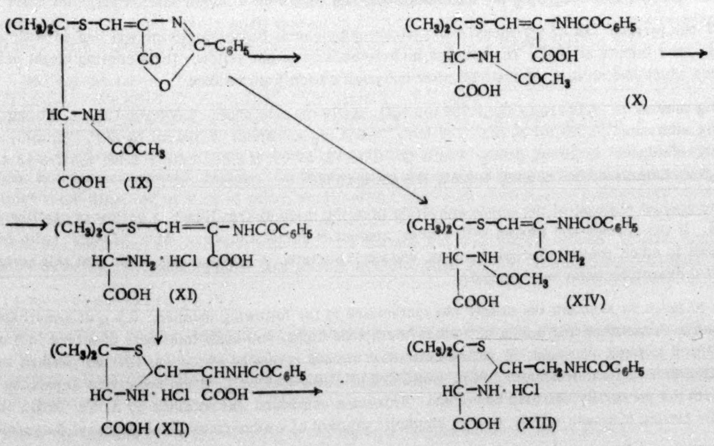
Therefore, a series of previously published papers and the present investigation make possible the conclusion that the cyclization of the oxazolone ring is accompanied by the redistribution of the energy of chemical affinity, and for this reason the molecule tends to be transformed into an unsaturated oxazolone with conjugated double bonds. In relation to their possibility, this or other change in their structure occurs.

Upon dissolving S(2-phenyl-5-oxazolonemethylene-4)-N-acetylpenicillamine (IX) in concentrated ammonia solution, the light yellow color of the solution characteristic for oxazolones, disappears rapidly. α-Benzoylamino-β-S(N-acetylpenicillamine)acrylic amide could be isolated from the reaction mass in the form of the benzylamine salt.

Concentrated hydrochloric acid also splits the oxazolone and forms α-benzoylamino-β-S(N-acetylpenicillamine)acrylic acid (X) which was isolated in the form of the dibenzylamine salt.

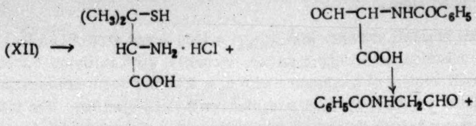
The evolution of carbon dioxide could not be observed upon heating (X) in the dry state, as well as in aqueous solution, which can be explained by the stability of a carboxyl attached to an ethylenic group in (X). Conversely, heating (IX), (X) and (XIV) with 2 N hydrochloric acid is accompanied by the evolution of carbon dioxide and the crystallization of phenylpenicilloinic acid hydrochloride (XIII).

The process of its formation is represented by the following scheme:



From the scheme it is apparent that the disruption of the oxazolone ring (X) occurs first, then the cleavage of the acetyl group (XI), the closing of the thiazolidine ring (XII), and finally, the decarboxylation of the substance.

The closing thiazolidine ring precedes the carboxylation process, and a state of dynamic equilibrium is established in the solution when part of the phenylpenicilloinic acid hydrochloride (XII) decomposes into penicillamine hydrochloride and the unstable formylhippuric acid. The latter easily decomposes on heating into benzoylaminoacetaldehyde and carbon dioxide:



$$(XII) \longrightarrow \begin{array}{c}(CH_3)_2C{-}SH\\ |\\ HC{-}NH_2\cdot HCl\\ |\\ COOH\end{array} + \begin{array}{c}OCH{-}CH{-}NHCOC_6H_5\\ |\\ COOH\\ \downarrow\\ C_6H_5CONHCH_2CHO + CO_2\end{array}$$

Benzoylaminoacetaldehyde reacts with penicillamine hydrochloride to form the difficultly soluble in dilute hydrochloric acid, phenylpenicillainic acid hydrochloride with m.p. 216-217° (with decomp.). In order to prove its structure, it was compared with phenylpenicillainic acid hydrochloride reported in the literature [10] prepared by the condensation of dl-penicillamine hydrochloride with the diethylacetal of formylhippuric acid. The character of the crystals, the absence of a depression in melting point, and analysis left no doubt of the identity of both compounds.

The transformation of S(2-phenyl-5-oxazolonemethylene-4)-N-acetylpenicillamine into phenylpenicillainic acid hydrochloride serves as proof of the formation of the thiazolidine ring by the addition of the amino group to the C=C bond, found attached to the sulfur atom, which previously has been mentioned in communications II [11] and IV [6]. In all truth, this is a general reaction for the preparation of thiazolidine compounds.

EXPERIMENTAL

Reaction of Acetic Anhydride with S(2-Phenyl-5-oxazolonemethylene-4)-N-acetylpenicillamine

0.2 g of S(2-phenyl-5-oxazolonemethylene-4)-N-acetylpenicillamine was heated with 2 ml of acetic anhydride for 10 minutes on the boiling water bath. Upon cooling, yellow needles separated which had an m.p. 174-176° after recrystallization from toluene. It is soluble in alcohol, acetone, ethyl acetate, and acetic anhydride.

6.757 mg substance: 0.341 ml N_2 (28°, 750 mm). 5.604 mg substance: 0.275 ml N_2 (26°, 726 mm). Found %: N 5.49, 5.35. $C_{12}H_9O_3NS$. Calculated %: N 5.66.

0.2 g of the pyridine salt of S(2-phenyl-5-oxazolonemethylene-4)-N-acetylcysteine was heated with 3 ml of acetic anhydride for 1 minute at 100°. The reaction mixture became bright yellow. Upon cooling bright yellow needles separated which had an m.p. of 174-176° after recrystallization from toluene.

3.728 mg substance: 7.984 mg CO_2; 1.229 mg H_2O. 3.613 mg substance: 7.670 mg CO_2; 1.180 mg H_2O. 7.917 mg substance: 0.394 ml N_2 (23°, 732 mm). 7.855 mg substance: 0.394 ml N_2 (23°, 732 mm). 5.187 mg substance: 4.710 mg $BaSO_4$. Found %: C 58.48, 57.93; H 3.69, 3.65; N 5.53, 5.57; S 12.48. $C_{12}H_9O_3NS$. Calculated %: C 58.3, H 3.67; N 5.66; S 12.95.

After the gradual removal of the acetic anhydride from the main mother liquor, a yellow crystalline substance appeared. It was filtered and washed with a small amount of acetic anhydride; m.p. 230-232° (with decomp.). It is poorly soluble in ether, methyl alcohol, acetone, and ethyl acetate. A proposal was made that this compound was bis(2-phenyl-5-oxazolonemethylene-4)sulfide.

In order to prove its structure the sulfide was synthesized in the following manner: 0.5 g of 4-mercaptomethylene-2-phenyl-5-oxazolone and 0.55 g of 4-ethoxymethylene-2-phenyl-5-oxazolone were dissolved in 2 ml of pyridine and allowed to stand overnight. A yellow crystalline residue separated which was filtered, washed with pyridine, and dried in a vacuum desiccator. M.p. was 233-235° (with decomp.). It did not give a depression in melting point with the previously obtained compound. This same compound was obtained by A. Ya. Berlin and V. I. Maimind by passing hydrogen sulfide into an alcoholic solution of 4-ethoxymethylene-2-phenyl-5-oxazolone [7].

0.7 g of 4-mercaptomethylene-2-phenyl-5-oxazolone was heated with 10 ml of acetic anhydride for 1 minute at 100°. Upon cooling, crystals of 4-acetothiomethylene-2-phenyl-5-oxazolone separated which were recrystallized from toluene. M.p. 174-176°. Bright yellow needles.

3.402 mg substance: 7.295 mg CO_2; 1.132 mg H_2O. 7.618 mg substance: 0.378 ml N_2 (23°, 730 mm). 6.855 mg substance: 0.349 ml N_2 (23°, 730 mm). Found %: C 58.51; H 3.72; N 5.50, 5.64. $C_{12}H_9O_3NS$. Calculated %: C 58.3; H 3.67; N 5.66.

All three samples of 4-acetothiomethylene-2-phenyl-5-oxazolone, obtained from various compounds, did not give a depression in melting point.

S(2-Phenyl-5-oxazolonemethylene-4)-N-benzoylpenicillamine (VI).

1 g of N-benzoylpenicillamine, 0.86 g of 4-ethoxymethylene-2-phenyl-5-oxazolone in 5 g of dry pyridine were heated for 12 hours at 80°. The reaction mixture was poured into 200 ml of ether and was shaken with 40 ml of 10% sulfuric acid. The ether solution was separated, washed with water, and then the S(2-phenyl-5-oxazolonemethylene-4)-N-benzoylpenicillamine was extracted from the ether solution with 10 ml of 5% sodium carbonate solution. The substance was once more transferred into 100 ml of ether from the aqueous solution upon acidification with 10% sulfuric acid. After washing the ether solution with water, drying with magnesium sulfate, and the removal of the ether on the water bath, a thick yellow oil remained. Upon drying in a vacuum desiccator, it was transformed into a hard yellow amorphous mass with m.p. 82-85°. It was very soluble in ether, alcohol, acetone, chloroform, and ethylacetate; it was insoluble in benzene.

6.430 mg substance: 0.353 ml N_2 (32°, 730 mm). Found %: N 6.08. $C_{22}H_{20}O_5N_2S$. Calculated %: N 6.6.

Reaction of Acetic Anhydride with S(2-Phenyl-5-oxazolonemethylene-4)-N-benzoylpenicillamine.

1 g of S(2-phenyl-5-oxazolonemethylene-4)-N-benzoylpenicillamine was heated with 7 ml of acetic anhydride for 2 minutes at 100°. Upon cooling, bright yellow needles of 4-acetothiomethylene-2-phenyl-5-oxazolone separated which were recrystallized from toluene. M.p. 174-176°. The mother liquor was evaporated in vacuum in order to remove the acetic anhydride, and the residual oil dissolved in 5 ml of ethyl alcohol. Upon cooling, a small amount more of the crystals separated. The crystals were filtered and recrystallized 2 times from toluene. Bright yellow needles with m.p. 170-172°. From the second mother liquor, a small amount more of the crystals with m.p. 168-170° was isolated upon evaporation to a small volume. Analysis of the substance with m.p. 174-176°.

7.902 mg substance: 0.406 ml N_2 (22°, 729 mm). 9.082 mg substance: 0.457 ml N_2 (22°, 729 mm). 3.545 mg substance: 3.203 mg $BaSO_4$. Found %: N 5.70, 5.59; S 12.42. $C_{12}H_9O_3NS$. Calculated %: N 5.66; S 12.95.

From the third mother liquor, a substance, in the form of light yellow thin needles, slowly crystallized. It was recrystallized 2 times from a small amount of alcohol. M.p. 96-98°. It did not give a depression in melting point with 4-isopropylidene-2-phenyl-5-oxazolone prepared by a known method [8].

7.387 mg substance: 0.456 ml N_2 (23°, 732 mm) 5.665 mg substance: 0.360 ml N_2 (23°, 732 mm). Found %: N 6.86, 7.06. $C_{12}H_{11}O_2N$. Calculated %: N 6.96.

α-Benzoylamino-β-S(N-Acetylpenicillamine)acrylic Amide (XIV).

0.5 g S(2-phenyl-5-oxazolonemethylene-4)-N-acetylpenicillamine was dissolved in 5 ml of aqueous ammonia. The yellow solution decolorized rapidly. On the next day, the solution was evaporated in vacuum to dryness, the residue once more dissolved in 5 ml of water, acidified to Congo with concentrated hydrochloric acid, and once more evaporated in vacuum to dryness. The dry substance was then dissolved in 10 ml of acetone, and the insoluble residue of ammonium chloride was filtered. The acetone was removed in vacuum. A solid amorphous mass, insoluble in water, alcohol, and acetone, and soluble in ether, ethyl acetate, and toluene, remained.

Benzylammonium Salt (XIV)

The amorphous powder obtained was dissolved in 4 ml of acetone and treated with 0.2 g of benzylamine. The oil which separated, crystallized rapidly. The crystals were filtered, washed with acetone, and dissolved in 2 ml of alcohol. Upon the addition, of 3 ml of acetone to solution, the crystallization of a substance in the form of nodules with m.p. 138°.

3.888 mg substance: 8.364 mg CO_2, 2.142 mg H_2O. Found %: C 58.70; H 6.16. $C_{24}H_{30}O_5N_4S$. Calculated %: C 59.26; H 6.22.

α-Benzoylamino-β-S(N-Acetylpenicillamine)acrylic Acid (X).

0.6 g of S(2-phenyl-5-oxazolonemethylene-4)-N-acetylpenicillamine was dissolved in 2 ml of concentrated hydrochloric acid. After 1 hour, the solution was practically decolorized. On the next day, the solution, was evaporated in a vacuum desiccator. A white powder, readily soluble in water, alcohol, acetone, and dioxane, was obtained. It melted at 123-135° (without the separation of carbon dioxide). An 0.1 N solution of iodine was not titrated (reaction for the absence of a thiazolidine ring).

After a prolonged storage in the vacuum desiccator over sodium hydroxide, 0.2 g of the substance was dissolved in 2 ml of water, and the solution heated on the boiling water bath. The separation of carbon dioxide was not observed (absence of clouding in a barium hydroxide solution.).

0.0955 g substance: 5.1 ml 0.1 N NaOH. Found %: CO_2- groups 24.03. $C_{17}H_{20}O_6N_2S$. Calculated %: CO_2- groups 23.68.

Dibenzylamino Salt (X).

0.5 g of α-benzoylamino-β-S(N-acetylpenicillamine)acrylic acid was dissolved in 5 ml of acetone and 0.2 g of benzylamine was added. A white crystalline residue separated rapidly, which was filtered, dissolved in 2 ml of alcohol, and after the addition of 8 ml of acetone, it was left to crystallize. Colorless spherical crystals of needles with m.p. 148-150° (with decomp.).

4.188 mg substance: 9.599 mg CO_2; 2.732 mg H_2O. 3.914 mg substance: 8.895 mg CO_2; 2.288 mg H_2O. 7.210 mg substance: 0.579 ml N_2 (21°, 736.6 mm). Found %: C 62.28, 62.22; H 6.34, 6.54; N 9.03; S 5.42. $C_{31}H_{38}O_6N_4S$. Calculated %: C 62.58; H 6.44; N 9.42; S 5.38.

Phenylpenicilloinic Acid Hydrochloride (XIII)

0.3 g of S(2-phenyl-5-oxazolonemethylene-4)-N-acetylpenicillamine was heated for 3 hours on the boiling water bath with 5 ml of 1.5 N hydrochloric acid. Reaction was accompanied by the separation of carbon dioxide. Upon cooling, coarse crystals separated. They were dissolved in a small amount of boiling water, the solution treated with carbon, and filtered. Upon the acidification of the solution with concentrated hydrochloric acid, phenylpenicilloinic acid hydrochloride with m.p. 215-216° (with decomp.) crystallized rapidly. It did not give a depression in melting point with an authentic sample prepared from penicillamine hydrochloride and the diethylacetal of formylhippuric acid.

Phenylpenicillainic acid hydrochloride was also obtained upon heating α-benzoylamino-β-S(N-acetylpenicillamine)acrylic acid (X) and its amide (XIV) with 2 N hydrochloric acid.

SUMMARY

1. 4-Isopropylidene-2-phenyl-5-oxazolone and 4-acetothiomethylene-2-phenyl-5-oxazolone were formed by the action of acetic anhydride on S(2-phenyl-5-oxazolonemethylene-4)-N-benzoylpenicillamine. It was proposed that the reaction proceeds through a stage of the formation of an unstable compound with two oxazolone rings which very easily split into two unsaturated oxazolones.

2. It was shown that when the oxazolone ring is closed, the substance tends to be converted into a more stable system with conjugated double bonds. Some examples are cited from the literature.

3. A mechanism was given for the transformation reaction of S(2-phenyl-5-oxazolonemethylene-4)-N-acetylpenicillamine into phenylpenicilloinic acid hydrochloride.

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* See Consultants Bureau English trans. p. 2251.

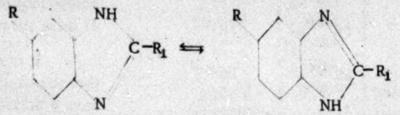
** See Consultants Bureau English trans. 1077.

INVESTIGATION OF IMIDAZOLE DERIVATIVES

V. AMPHOTERIC CHARACTER OF BENZIMIDAZOLE DERIVATIVES AND THEIR TAUTOMERIC TRANSFORMATIONS [1]

L. S. Efros and B. A. Porai-Koshits

In one of the previous communications [2] it was proposed that the ease of tautomeric transformations of benzimidazole derivatives, which was found by a series of investigations [3] and occurs according to the following scheme:



is explained by the amphoteric character of these substances.

In order to prove the proposal, the potentiometric titration (with glass electrodes) of benzimidazole derivatives was undertaken.

Curves with two clear potential jumps were obtained by the titration of benzimidazole, its 2-methyl-, 2-phenyl, and 2-benzyl derivatives, which are reported in the experimental part of this paper. The calculation of the dissociation constant, effected from these curves if the imidazole derivatives are considered as being only bases, showed a considerable disagreement with the values calculated from the hydrolysis of salts, from the isoelectric point, and from the half equivalent point. This disagreement exceeds by many times, the possible experimental error (Table 1) and showed that benzimidazole derivatives are not to be viewed as only being bases. For this reason, a recalculation was made considering these compounds to be amphoteric. By finding the acidity constant of the benzimidazole derivatives from the hydrolysis of the alkali salts and the corresponding half equivalent points, and considering that, at the isoelectric points, these substances exist in the form of salts formed by weak acids and bases, basic constants were calculated and agreed within experimental error with the results of the calculations by means of other points in the curve (Table 1).

TABLE 1

Substance investigated	Calculated constants without accounting for the amphoteric properties			Calculated constants taking into account amphoteric properties		
	Basicity			Basicity		Acidity
	by hydrolysis of the salt	by the isoelectric point	by the half equivalent point	by hydrolysis of the salt and half equivalent point	by the isoelectric point	by hydrolysis of the alkali salt and half equiv. point
Benzimidazole	$10^{-8.6}$	$10^{-10.4}$	$10^{-8.5}$	$10^{-8.6}$	$10^{-8.7}$	$10^{-12.7}$
2-Methylbenzimidazole	$10^{-8.3}$	$10^{-10.0}$	$10^{-8.3}$	$10^{-8.3}$	$10^{-8.3}$	$10^{-10.5}$
2-Phenylbenzimidazole	$10^{-9.2}$	$10^{-8.4}$	$10^{-9.3}$	$10^{-9.2}$	$10^{-9.2}$	$10^{-12.5}$
2-Benzylbenzimidazole	$10^{-8.9}$	$10^{-6.2}$	$10^{-8.8}$	$10^{-8.9}$	$10^{-8.9}$	$10^{-12.7}$

This agreement proves, therefore, that the benzimidazole derivatives being studied are actually amphoteric substances.

Nevertheless, it seemed desirable for comparison and for proof of the correctness of the chosen method, to effect potentiometric titrations of such imidazole derivatives in which the hydrogen in the imino group was substituted by an organic radical. It is clear that these compounds, in contrast to the previously studied, must only possess basic properties.

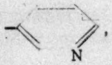
Upon the potentiometric titration of the N-β-cyanoethylbenzimidazole (I) synthesized and its 2-methyl derivative (II), curves were obtained, given in Figs. 3 and 4, with two clear potential jumps, the distance between which strictly corresponded to one equivalent of alkali. The calculation of the basic constant of these compounds, as was expected, gave complete agreement of the values found with hydrolysis of the salt, the isoelectric point, and the half equivalent point, which indicated the absence of amphoteric properties in N-substituted benzimidazole derivatives, and at the same time proved the correctness of the chosen method (Table 2).

TABLE 2

Substance obtained	Calculated basic constants		
	By hydrolysis of the salt	By the isoelectric point	By means of the half equivalent point
1-Cyanoethylbenzimidazole	$10^{-9.7}$	$10^{-9.6}$	$10^{-9.7}$
1-Cyanoethyl-2-methylbenzimidazole	$10^{-8.3}$	$10^{-8.3}$	$10^{-8.4}$

In order more completely to know the basic and acidic properties of benzimidazole derivatives, and the effect of various substituents on these properties, a potentiometric titration was conducted for a series of other compounds of this group. The results of these titrations are given in Table 3.

It is apparent from Table 3, that substituents found in position 2 have a noticeable effect on the basic constants of benzimidazoles, and they are arranged in the following series in the order of decreasing basic constants.

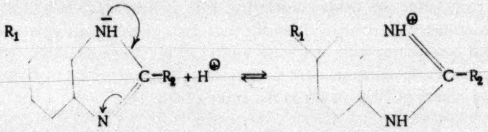
$N(CH_3)_2$, $CH_2{-}CH_2{-}C_6H_5$, CH_3, CH_2OH, H, $CH{=}CH{-}C_6H_5$, $CH_2{-}C_6H_5$, C_6H_5, CH_2OCOCH_3, , Cl

$$\xrightarrow{\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad}$$

Substituents in position 5 (6) are arranged in the following series, correspondingly:

NH_2, CH_3, H, NO_2.

These observations found a simple interpretation upon examining the salt-forming reactions of benzimidazole derivatives:



It is evident that the benzimidazole derivatives will be more basic, the greater the stability possessed by the cation formed. The stability of this cation depends on how equally distributed the positive charge is within it, and the substituents.

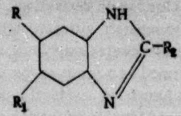
Therefore, if the substituents contributes to the equalization of the electron density in the ion, repelling electrons from itself, it increases the basicity of the compound; by the reverse action, on the other hand, the basic constant is decreased. From the above it is seen that, in the previously reported series, the substituents placed to the left of H repel electrons, to the right, attract. Among the compounds studied with substituents in position 2, the maximum electron repulsion activity is possessed by the dimethylamino group, the basic constant is increased 100-fold; the maximum reverse effect is possessed by chorine which decreases this constant 1000 times.

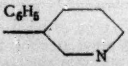
As it was expected, the CH_3 group posesses a weakly expressed electron repelling action. This action is weakened by the introduction of an alcoholic hydroxyl group into it, and it becomes electron attracting after the introduction of an alkyl residue into it. The phenyl residue attracts electrons, but its effect is weakened if an intermediate CH_2 is put in, and completely disappears if the phenyl radical is separated from the ring by a two-CH_2-group chain. Conversely, if the phenyl radical is separated from the ring by two carbon atoms with a double bond through which conjugation is possible, its electron attracting action is retained. Substituents found in position 5, analogously, affect the basicity of the benzimidazoles by means of systems of conjugated double bonds.

Starting from the above, certain theoretical conclusions can be drawn on the possible mechanism of the tautometric transformations of these compounds resulting from their amphoteric properties.

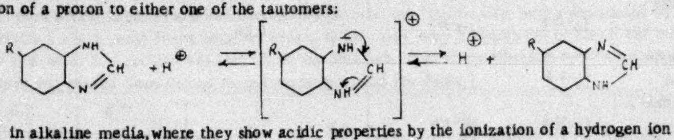
TABLE 3

Basicity and Acidity of Compounds of the General Formula

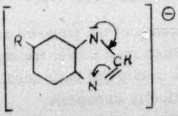


No.	R	R₁	R₂	K-basic	K-acidic	Notes
1	H	H	H	$10^{-8.6}$	$10^{-12.7}$	
2	H	H	OH	$10^{-11.6}$	$10^{-12.7}$	
3	H	H	Cl	$10^{-11.4}$	$10^{-9.6}$	
4	H	H	$N(CH_3)_2$	$10^{-6.6}$	$10^{-11.5}$	
5	H	H	CH_3	$10^{-8.3}$	$10^{-10.5}$	
6	H	H	CH_2OH	$10^{-8.4}$	$10^{-10.6}$	
7	H	H	CH_2OCOCH_3	$10^{-9.4}$	$10^{-11.7}$	
8	H	H	$CH_2N(C_2H_5)_2$	$10^{-6.2}$ $10^{-11.3}$	$10^{-12.1}$	The first basic constant, evidently, is due to the diethylamino group.
9	H	H	C_6H_5	$10^{-9.2}$	$10^{-12.5}$	
10	H	H		$10^{-10.2}$ $10^{-11.3}$	$10^{-11.1}$	One of the basic constants, evidently, the second, is due to the nitrogen of the pyridine ring.
11	H	H	$CH_2-C_6H_5$	$10^{-8.9}$	$10^{-12.7}$	
12	H	H	$CH_2CH_2C_6H_5$	$10^{-7.9}$	$10^{-11.4}$	
13	H	H	$CH{=}CH-C_6H_5$	$10^{-8.8}$	$10^{-11.3}$	
14	NO_2	H	H	$10^{-10.0}$	$10^{-11.2}$	
15	NH_2	H	H	$10^{-7.4}$ $10^{-10.7}$	$10^{-11.2}$	The second basic constant must be due to the amino group
16	CH_3	H	CH_3	$10^{-8.0}$	$10^{-11.2}$	
17	NO_2	H	CH_3	$10^{-9.7}$	$10^{-10.0}$	
18	NO_2	NO_2	CH_3	$10^{-11.2}$	$10^{-9.7}$	
19	NH_2	NH_2	CH_3	$10^{-6.5}$ $10^{-10.7}$ $10^{-11.9}$	$10^{-10.9}$	The second and third basic constants are due to the amino groups
20	CH_3	H	$CH_2-C_6H_5$	10^{-8}	$10^{-11.2}$	

Because of these properties, tautomeric transformations of benzimidazole derivatives can occur in acidic media, where the substances behave as bases and form the same cation with an equalized electron density by the addition of a proton to either one of the tautomers:

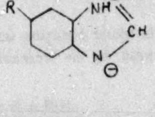


as well as in alkaline media, where they show acidic properties by the ionization of a hydrogen ion to form a common anion for both the tautomers:

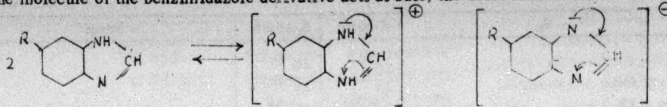


However, particular attention is merited by the behavior of benzimidazole derivatives at the isoelectric point, in which, as it is shown above, these compounds form salts of weak acids and weak bases.

It could have been supposed that, like amino acids, these salts are intramolecular and have the following structure:



But in the amino acids, as is known, the carrier of the basic properties is the amino group, and the acidic, the carboxyl, whereas in benzimidazole derivatives, the basic and acidic properties as a result of the effect of conjugation, cannot be assigned to separate nitrogen atoms and are determined by the structure of the molecule as a whole. For this reason, the intramolecular amphionic structure of the salts appeared to be scarcely probable. It is believed that these salts are formed as a result of the intermolecular reaction and consist of the previously represented cations and anions. Their formation, evidently, must occur according to the following equilibrium reaction, in which one molecule of the benzimidazole derivative acts as base, the other as an acid.



It could have been thought that, in the presence of equimolecular quantities of the different benzimidazole derivatives in the solution which differ considerably from each other in the degree of acidity and basicity, these (if, as it was thought, they were intermolecular) must be formed from the cation of the more basic benzimidazole, and the anion of the more acidic compound. These conditions could be achieved by the proper choice of the starting substances by means of pH measurement of the solutions obtained.

In order to solve this problem, pairs of compounds were chosen from the data in Table 3, the investigation of whose solutions could give an answer to the given problem.

Accurate samples of these substances (0.001 mole) were dissolved in 40% ethyl alcohol, the pH of these solutions was measured, and the solutions were combined in pairs and the pH of the resulting solution measured once more. The results found were compared with the calculated (Table 4).

It is apparent from Table 4, that the pH of solutions obtained by the combination of the chosen benzimidazole derivatives, within the limits of error of measurement, coincide with the values calculated for salts formed according to the above equations.

TABLE 4

Starting point	K Basic	K Acidic	pH of starting solution		pH of combined solution	
			Found	Calculated	Found	calculated for intermolecular salts
I 2-Methylbenzimidazole . . .	$10^{-8.3}$	$10^{-10.5}$	8.0	8.1	7.7	7.7
5,6-Dinitro-2-methylbenzimidazole	$10^{-11.2}$	$10^{-9.7}$	6.3	6.25		
II 2,5-Dimethylbenzimidazole. . .	$10^{-8.0}$	$10^{-11.2}$	8.6	8.6	7.8	7.8
2-Chlorobenzimidazole	$10^{-11.4}$	$10^{-9.6}$	6.2	6.1		

These results, therefore, confirmed the existence of the proposed equilibrium reaction occurring at the isoelectric point. The existence of such an equilibrium must hinder the separation of desmotropic benzimidazole derivatives at the isoelectric point.* As for the acidic and basic media, in these, as is apparent from the above, the separation of separate tautomers is practically impossible.

This summary explains the reason for the lack of success of all investigators who tried to separate desmotropic forms of benzimidazole derivatives [8]. The main reason, as the author believes, is found in the amphoteric character of these substances.

The synthesis of the majority of the benzimidazole derivatives used in the investigation has previously been described in the literature. As for the N-derivatives described previously, the cyano-ethylation [4] of benzimidazole derivatives was studied as a means of preparing them*, which, according to one patent, can occur by the reaction of benzimidazole with acrylonitrile in the presence of sodium ethylate [5]. It was found, however, that this reaction did not occur under the conditions reported in the patent; the desired compound of structure I could only be obtained when trimethylphenylammonium hydroxide, as recommended by V. M. Rodionov and Yartseva [6], was used as the catalyst. In the presence of this catalyst, the reaction went in the cold, and cyanoethylbenzimidazole (I) was obtained in good yield, whose structure was confirmed by reactions, elementary analysis, potentiometric titration, as well as by hydrolysis with barium hydroxide, as a result of which the barium salt of the acid was obtained.

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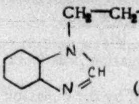
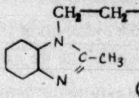
* It may be assumed that this equilibrium reaction, in whose equation water does not participate, can also occur in non-aqueous media; this was proved, for example, by the presence of molecular association of benzimidazole derivatives in naphthalene solutions [7].



(I)



(II)

Cyanoethyl derivatives of 2-methylbenzimidazole (II) and the the barium salt of the corresponding acid were obtained under analogous conditions.

However, here, the cyanoethylation reaction proceeded with somewhat greater difficulty than in the previous case: in order to effect it, for example, refluxing was necessary.

The cyanoethylation reaction could not be effected under these conditions with 2-phenyl- and 2-benzylbenzimidazol. The reaction did not occur, and the starting products were recovered unchanged in all cases.

By the way, it is of interest to mention that cyanoethylbenzimidazole (I) and especially, the acid, very easily eliminate an acrylic acid residue upon heating with acids and bases, and is converted into benzimidazole. The corresponding derivative of 2-methylbenzimidazole are, on the other hand, considerably more stable substances which could not be cleaved, even by prolonged heating with 20% hydrochloric acid in a sealed tube at 200°.

EXPERIMENTAL

I. Potentiometric Titration of Benzimidazole Derivatives

The potentiometric titration of benzimidazole derivatives was conducted with a vacuum tube potentiometer of the system GIPKh with glass electrodes. The latter, after preparation, were washed in hydrochloric acid and calibrated with accurate standard buffer solution. The straight line relation between the conditional millivolts and the pH of the solution obtained, enable the concentration of the hydrogen ions to be found at any point of the curves obtained. Inflection points on the curve were found by the graphic method of constructing tangents and were checked by calculation. In this way, points designated on the curves by the numbers 1 and 2 were found, between which, in all cases, only 1 equivalent of alkali had been consumed. In order to find point 3, a section was laid off on the absicissa equal to the distance between point 1 and 2, and a perpendicular was placed from its end to an intersection with the curve.

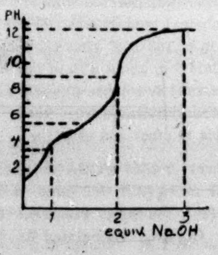


Fig. 1. Titration of benzimidazole.
1) pH 3.4; 2) pH 9.05; 3) pH 12.5

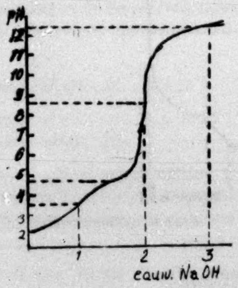


Fig. 2. Titration of 2-phenylbenzimidazole.
1) pH 3.5; 2) pH 8.7; 3) pH 12.5

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* This portion of the work was performed by K. B. Rall.

The calculation of the dissociation constants was done by applying the usual formulas derived from the mass action laws. Here, if the substance was considered to be only a base, then at point 1 it was looked upon as being in the form of the hydrochloride, from the hydrolysis of which was calculated the basic constant by the formula $K_0 = \frac{K_B \cdot C}{[H]^2}$. At point 2, this substance was looked upon as existing in the form of the free base, and in this case, the basic constant was calculated by the formula $K_0 = \frac{[OH]^2}{C}$. In the case where the substance was considered amphoteric, the calculation of the constants was somewhat changed.

The basic constant was found from point 1 as in the previous case. At point 2, it was considered that the substance existed in the form of a salt formed by a weak acid and a weak base, and the basic constant was found by the equation derived from the hydrolysis of this salt: $K_0 = \frac{K_B \cdot K_A}{[H]^2}$

The acidic constant (K_A), necessary for the calculation of this equation, was found from point 3 at which the amphoteric compound must exist in the form of the sodium salt, by the equation $K_A = \frac{K_B \cdot C}{[OH]^2}$, and from the corresponding half equivalent point.

1. Titration of Benzimidazole. A sample of 0.1584 g was dissolved in 20 ml of 0.1037 N hydrochloric acid, and titrated with an 0.086 N sodium hydroxide solution. A curve was obtained which is given in Fig. 1.

At point 1: pH 3.4, c $4.6 \cdot 10^{-2}$; at the half equivalent point pH 5.55; at point 2: pH 9.05, c $3 \cdot 10^{-2}$; at point 3: pH 12.5, c $2.2\ 10^{-2}$. The constants calculated by both methods are given in Table 1.

2. Titration of 2-Phenylbenzimidazole. The poor stability of this substance in water forced the titration to be effected, in this and the following cases, in an aqueous alcoholic mixture, which practically had no effect on the results of the determination.

0.2182 g of 2-phenylbenzimidazole hydrochloride was dissolved in 102 ml of 50% alcohol and 5 ml of 0.1 N hydrochloric acid. The titration was done with 0.1 N sodium hydroxide solution, and the curve given in Fig. 2 was obtained.

At point 1: pH 3.5, c $0.8 \cdot 10^{-2}$; at the half equivalent point: pH 4.75; at point 2: pH 8.7, c $0.63 \cdot 10^{-2}$; at point 3: pH 12.5, c $0.6 \cdot 10^{-2}$. The calculated constants are given in Table 1.

The titration of all of the other compounds was effected in a similar manner; the acidity and basicity constants of these are given in the theoretical section of the present communication.

II. Cyanoethylation of Benzimidazole

5 g of benzimidazole and 0.5 g of trimethylphenylammonium hydroxide in an alcoholic solution [6] were placed into a three necked flask equipped with a reflux condenser, dropping funnel, and thermometer, and were heated to 30-40°. At this temperature, 3.3 g of acrylonitrile (50% excess) was added gradually and the solution was allowed to cool and poured into a beaker containing 100 ml of water. In a short time, crystals of 1-cyanoethylbenzimidazole began to form, which were filtered. The mother liquor had to be evaporated since a considerable amount more of the product was isolated from it. The melting point of the technical product was 105-106° and increased to a constant m.p. 108-109° after 1-2 recrystallizations from water. Yield 6 g, about 83% of the theoretical. Colorless needles, readily soluble in warm alcohol, dilute acids, can be recrystallized from water, benzene, toluene, and are insoluble in ether and gasoline.

0.1427 g substance: 0.3658 g CO_2; 0.0684 g H_2O. 0.1005 g substance: 21.2 ml N_2 (21°, 762 mm). 0.0988 g substance: 20.9 ml N_2 (20°, 766 mm). Found %: C 69.95; H 5.36; N 24.67, 24.58. $C_{10}H_9N_3$. Calculated %: C 70.15; H 5.29, N 24.54.

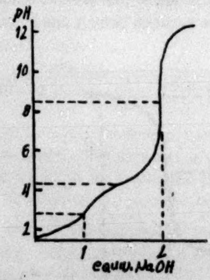

Fig. 3. Titration of 1-cyanoethylbenzimidazole. 1) pH 2.75; 2) pH 8.4.

Titration of 1-cyanoethylbenzimidazole was effected in the same manner as in the previous cases: 0.098 g of the substance was dissolved in 10 ml of 0.1037 N hydrochloric acid and titrated with 0.086 N sodium hydroxide (Fig. 3).

At point 1: pH 2.75, c $3.8 \cdot 10^{-2}$; at the half equivalent point: pH 4.3; at point 2: pH 8.4, c $2.5 \cdot 10^{-2}$. The calculated constants are given in Table 2. Consumption of alkali between points 1 and 2 was 6.8 ml. Found equivalent weight, 166. $C_{10}H_9N_3$. Calculated equivalent weight, 171.

The hydrolysis of the nitrile group of 1-cyanoethylbenzimidazole was effected in the following manner: 3 g of the substance was refluxed for 2 hours with a solution of 1.5 g of barium hydroxide, in 50 ml of water. In order to remove the excess barium hydroxide, a stream of carbon dioxide gas was passed through the cooled and filtered solutions, the residue was removed, and the solution was evaporated to dryness. 4.25 g, about 95% of the theoretical, of the barium salt of benzimidazolepropionic acid was obtained. It was a colorless crystalline substance which could be crystallized from a concentrated aqueous solution; the salt was readily soluble in alcohol.

0.1457 g substance: 0.2478 g CO_2; 0.0484 g H_2O. 0.0974 g substance: 9 ml N_2 (21°, 764 mm). 0.0879 g substance: 0.0394 g $BaSO_4$. 0.1724 g substance: 0.0773 g $BaSO_4$. Found %: C 46.41; H 3.71; N 10.78; Ba 26.37, 26.62. $C_{10}H_9O_2N_2Ba_{0.5}$. Calculated %: C 46.57; H 3.52; N 10.36 Ba 26.63.

The cleavage of 1-cyanoethylbenzimidazole and the corresponding acid obtained from it by the action of acids and bases, was also studied. It was found that an hour's boiling of these compounds with a 10% sodium hydroxide solution (1 g of the substance and 25 ml of the alkaline solution) led to the cleavage of the propionic acid residue and to the formation of benzimidazole. The latter isolated from the solution upon evaporation had a m.p. 168°, and did not give a depression when mixed with the authentic product.

An hour's heating of 1-cyanoethylbenzimidazole with a 20% hydrochloric acid solution led to the decomposition of this compound and the formation of benzimidazole, which occurred very rapidly by means of an intermediate hydrolysis of the nitrile group and the formation of the corresponding acid.

III. Cyanoethylation of 2-Methylbenzimidazole. 2 g of 2-methylbenzimidazole, 0.2 g of trimethylphenylammonium hydroxide in alcoholic solution, and 4-5 ml of ethyl alcohol were placed into a flask equipped with reflux condenser and dropping funnel, heated to boiling, and 1.2 g of acrylonitrile was added gradually to it; it was boiled for 1 hour more. After cooling, the solution was poured into 20-30 ml of water. Sometimes a precipitate formed after several hours, sometimes only after 24 hours of standing; m.p. 52-53°; it increased to 55-56° after recrystallization from water. The product contained water of crystallization which was removed on drying in a vacuum desiccator for several days. The melting point of the substance then increased to 89-90°. Yield, 1.9 g which was 70% of the theoretical.

1-Cyanoethyl-2-methylbenzimidazole was a colorless substance which recrystallized from water, benzene, and toluene, was readily soluble in alcohol, and insoluble in ether.

0.1241 g substance: 0.3241 g CO_2; 0.0679 g H_2O. 0.1002 g substance: 19.6 ml N_2 (24°, 764 mm). Found %: C 71.27; H 6.12; N 22.61. $C_{11}H_{11}N_3$. Calculated %: C 71.33; H 5.98; N 22.69.

The titration of 1-cyanoethyl-2-methylbenzimidazole was conducted as in the previous cases: 0.1240 g of the substance was dissolved in 20 ml of 0.1 N hydrochloric acid solution and titrated with 0.1 N sodium hydroxide solution (Fig. 4).

Point 1: pH 3.75, c $1.9 \cdot 10^{-2}$; half equivalent point: pH 5.7; point 2: pH 8.95, c $1.5 \cdot 10^{-2}$.

The calculated constants are given in Table 2. The consumption of alkali between points 1 and 2 was 6.8 ml. Equivalent weight found, 182. $C_{11}H_{11}N_3$. Calculated equivalent weight, 185.

The hydrolysis of the nitro group of this compound was effected in the following manner: 1.5 g of the nitrile was refluxed in a solution of 1.5 g of barium oxide in 50 ml of water for 2 hours. The isolation of the barium salt of the acid was effected in the same manner as in the previous case. Its yield was 1.9 g, about 86% of the theoretical. The salt was purified by precipitation with acetone from an aqueous solution.

0.1138 g substance: 10.2 ml N_2 (20°, 766 mm). 0.0832 g substance: 0.0355 g $BaSO_4$. Found %: N 10.52; Ba 25.12. $C_{11}H_{11}O_2N_2Ba_{0.5}$. Calculated %: N 10.33; Ba 25.26.

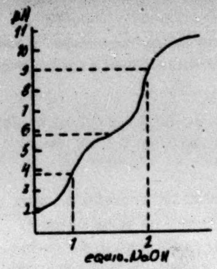

Fig. 4. Titration of 1-cyanoethyl-2-methylbenzimidazole.
1 - pH 3.75; 2 - pH 8.95

As in the previous case, the stability of the products obtained upon treatment with acids and alkali was studied. It was found that heating these compounds with 10, 20, and 30% hydrochloric acid, and even heating for 2 hours at 200° in a sealed tube did not lead to cleavage of the propionic acid and formation of 2-methylbenzimidazole.

SUMMARY

1. Derivatives of benzimidazole, not containing substituents on the nitrogen atom, were found to be amphoteric substances. The tautomers theoretically possible for these compounds formed identical cations in acidic solution, and identical anions in alkaline, while salts were formed at the isoelectric point which consisted of these cations and anions.

2. N-Cyanoethyl derivatives of these compounds were obtained by the action of acrylonitrile upon benzimidazole and its 2-methyl derivative, which, in contrast to the starting substances, did not possess acidic properties, and were only bases.

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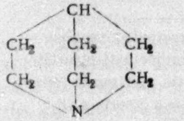
* See Consultants Bureau English Translation, page 1069.

** See Consultants Bureau English Translation, page 1063.

SYNTHESIS OF QUINUCLIDINE -2- CARBOXYLIC ACID

M. V. Rubtsov and M. I. Dorokhova

One of the structural parts of the quinine alkaloids is the quinuclidine ring which is a bicyclic system of the following structure:



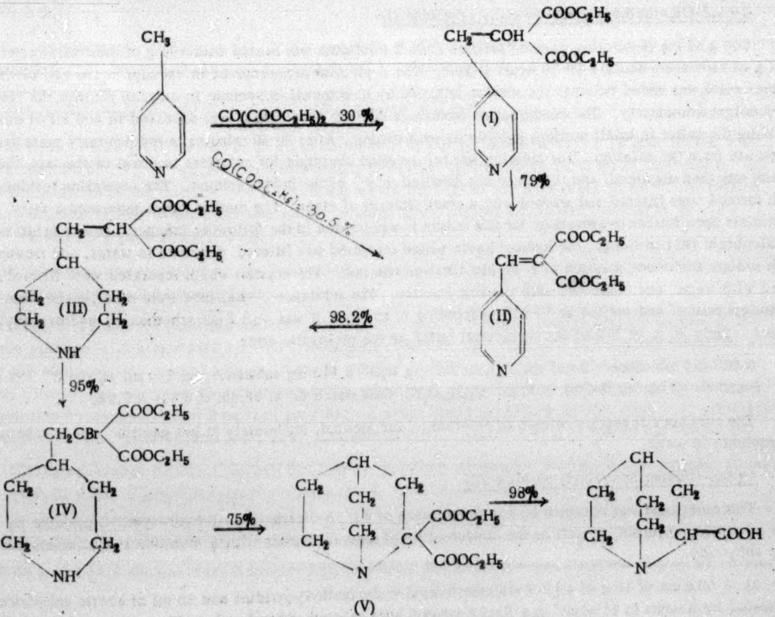
The synthesis of quinuclidine was accomplished in 1909 [1]. Certain of its homologs containing alkyl (methyl, ethyl) groups in position 2 [2] or 3 of the quinuclidine ring [3] have also been reported.

These compounds, however, are of limited interest since, as a result of their complicated synthesis, they cannot serve as starting material for the preparation of quinuclidine derivatives.

In 1937 a synthesis of quinuclidine-2-carboxylic acid was reported [4] which was accomplished in 12 stages.

Quinuclidine-2-carboxylic acid can serve as an excellent starting material for the preparation of various quinuclidine derivatives. However, the given method of synthesis is so complex that this interesting compound must be viewed as poorly available.

A new, simpler method for the preparation of quinuclidine-2-carboxylic acid was developed, which was accomplished in 5 stages according to the following scheme:



γ-Picoline and mesoxalic ester served as the starting product. In place of pure γ-picoline, a β-picoline fraction purified from 2,6-lutidine and consisting, approximately, of 60% β-picoline and 40% γ-picoline was used. Since β-picoline is unable to react with the carbonyl group its presence could not affect the course of the process essentially, as it participates as a solvent.

Upon the condensation of γ-picoline with mesoxalic ester in the presence of piperidine acetate, 4-(β,β-dicarbethoxy-β-hydroxyethyl)-pyridine (I) is formed in a yield of 30% of theory based on the mesoxalic ester. Compound (I) dehydrates and is transformed into 4-(β,β-dicarbethoxyvinyl)-pyridine (II) upon heating with acetic anhydride in a yield of 79% based on (I) and about 24% based on mesoxalic ester.

Later it was found that the ethylene derivative (II) could be obtained in a better yield (30.5%) and in one stage directly from γ-picoline and mesoxalic ester if the reaction is conducted in an acetic anhydride medium.

Upon the catalytic hydrogenation of the ethylene derivative (II), 4-(β,β-dicarbethoxyethyl)-piperidine (III) was obtained which was transformed in good yield (95%) into 4-(β,β-dicarbethoxy-β-bromoethyl)-piperidine (IV) by the action of bromine in a chloroform medium. The latter cyclizes upon heating with pyridine to form the diethyl ester of quinuclidine-2,2-dicarboxylic acid (V) in a 75% yield. This compound is a colorless oil boiling at 153-155°. (19 mm).

Upon heating with concentrated hydrochloric acid, a saponification occurs with a simultaneous decarboxylation, and quinuclidine-2-carboxylic acid is formed almost quantitatively.

The yield of quinuclidine-2-carboxylic acid in the form of the hydrochloride is 20% of theory based on the mesoxalic ester. 2-Bromoquinuclidine is formed by the action of bromine on the silver salt of quinuclidine carboxylic acid. The amide and nitrile were obtained from quinuclidinecarboxylic acid by means of the acid chloride.

EXPERIMENTAL

4-(β,β-Dicarbethoxy-β-hydroxyethyl) pyridine (I)

200 g of the β-picoline fraction purified from 2,6-lutidine was heated with 100 g of mesoxalic ester and 2 g of piperidine acetate for 12 hours at 100°. The β-picoline was removed in vacuum at the end of the heating; xylol was added twice to the residue followed by its removal in vacuum in order to remove the traces of β-picoline completely. The condensation product, a ductile, brown mass, was dissolved in 400 ml of ether by adding the latter in small portions (50-70 ml) with stirring. After 30-40 minutes, a reddish tarry mass began to separate from the solution. The solution was left to stand overnight for complete removal of the tars, the solution was then decanted, and the ether was distilled to $\frac{1}{4}$ of the initial volume. The crystaline residue which formed was filtered and washed with a small amount of ether. The mother liquor separated a tarry brown mass upon further evaporation; for this reason it was treated in the following manner: it was acidified with alcoholic HCl to Congo, the hydrochloride which separated was filtered, dissolved in water, and treated with a sodium carbonate solution to a weakly alkaline reaction. The crystals which separated were filtered, washed with water, and combined with the first fraction. The substance crystallized from ether in the form of colorless prisms, and melted at 79-80°. According to analysis, it was 4-(β,β-dicarbethoxy-β-hydroxyethyl) pyridine. Yield 46 g, or 30% of the theoretical based on the mesoxalic ester.

3.965 mg substance: 8.516 mg CO_2; 2.240 mg H_2O. 6.113 mg substance: 0.290 ml N_2 (24.5°, 732.8 mm). Found %: C 58.58; H 6.32; N 5.25. $C_{13}H_{17}O_5N$. Calculated %: C 58.40; H 6.41; N 5.24.

The substance is readily soluble in chloroform and alcohol, moderately in hot gasoline and in ether; it is insoluble in water.

4-(β,β-Dicarbethoxyvinyl) pyridine (II)

This compound was obtained by the dehydration of 4-(β,β-dicarbethoxy-β-hydroxyethyl)-pyridine by means of acetic anhydride, as well as the condensation of mesoxalic ester with γ-picoline in the presence of acetic anhydride.

a) A mixture of 10 g of 4-(β,β-dicarbethoxy-β-hydroxyethyl)-pyridine and 20 ml of acetic anhydride were heated for 2 hours at 115-120° in a flask equipped with calcium chloride tube. The acetic anhydride and the acetic acid formed during the reaction were removed in vacuum on the water bath, and the residue was distilled at 5 mm and a fraction boiling at 162-164° was collected. Yield 7.3 g or 79% of the theoretical. The substance was a colorless oil readily soluble in water.

d_4^{20} 1.1583; n_D^{20} 1.5176; MR_D 65.12. $C_{13}H_{15}O_4N$. Calculated MR_D 65.18.
3.621 mg substance: 8.325 mg CO_2: 1.954 mg H_2O. 3.280 mg substance: 0.412 ml N_2 (23°, 736 mm).
Found %: C 62.70; H 6.04; N 5.56. $C_{13}H_{15}O_4N$. Calculated %: C 62.62; H 6.07; N 5.62.

The hydrochloride was formed by the action of an alcoholic solution of hydrogen chloride on an ether solution of the base in the form of a snow white powder melting at 180-182°. It is readily soluble in water, chloroform, and in hot alcohol; it is insoluble in ether.

3.302 mg substance: 6.651 mg CO_2; 1.735 mg H_2O. 8.632 mg substance: 0.382 ml N_2 (18° 751 mm).
Found %: C 54.93; H 5.88; N 5.05. $C_{13}H_{15}O_4N \cdot HCl$. Calculated %: C 54.63; H 5.65; N 4.90.

b) A mixture of 17.4 g of the β-picoline fraction, purified from 2,6-lutidine, 17.4 g of mesoxalic ester and 17.4 g of acetic anhydride was heated for 9 hours at 90° in a flask equipped with a calcium chloride tube. Then the β-picoline, acetic acid, and excess acetic anhydride were removed in vacuum on the water bath, and the residue was distilled at 5 mm; a fraction boiling at 155-170° was collected. 9 g of a yellowish oil was obtained which was redistilled at the same pressure, collecting a fraction boiling at 162-164°. Yield 7.6 g or 30.5% of the theoretical.

4-(β,β-Dicarbethoxyethyl)-piperidine (III)

20 g of 4-(β,β-dicarbethoxyvinyl)-pyridine was mixed with 150 ml of absolute alcohol, 0.8 g of platinum oxide added, and subjected to hydrogenation under a pressure of 40-50 cm of a water column. The hydrogenation was completed within 15-20 hours. The catalyst was filtered, the filtrate evaporated to dryness in vacuum, the crystalline residue was dissolved in 30-35 ml of chloroform by heating, and precipitated by the addition of 5 parts, by volume, of dry ether.

Colorless, microscopic prisms, readily soluble in water, alcohol, and chloroform; m.p. 125-126°. Yield 20.2 g or 98.2 %.

3.857 mg substance: 7.538 mg CO_2; 2.923 mg H_2O. 5.726 mg substance: 0.241 ml N_2 (16.5°, 761 mm).
Found %: C 53.30; H 8.11; N 4.90. $C_{13}H_{23}O_4N \cdot HCl$. Calculated %: C 53.13; H 8.23; N 4.77.

4-(β,β-Dicarbethoxy-β-bromoethyl) piperidine hydrochloride (IV)

A solution of 8.25 g of bromine in 60 ml of chloroform was added dropwise over a 12 hour period with stirring to a solution of 15 g of 4-(β,β-dicarbethoxyethyl)-piperidine hydrochloride in 45 ml of chloroform. At the end of the addition of the bromine, the mixture was stirred for 2 hours and then about 75 ml of chloroform was distilled off, and 120 ml of dry ether was added. A white finely crystalline residue melting at 127-129° separated. Yield 19.8 g (instead of 19.03 g).

This substance was a mixture of the hydrochloride and hydrobromide 4-(β,β-dicarbethoxy-β-bromoethyl)-piperidine, which explains the increased yield.

In order to prepare the pure hydrochloride, the mixture obtined was dissolved in a small amount of ice water, made alkaline with a saturated solution of potassium carbonate, the separated base rapidly extracted with ether, and the ether solution treated with an alcoholic solution of hydrogen chloride. The hydrochloride which formed was filtered, and air dried, then dissolved in dry chloroform, filtered from a turbidity, and precipitated from the solution by the addition of 2 parts of dry ether. A white finely crystalline powder with m.p. 138.5-140°; readily soluble in water, alcohol, and chloroform; insoluble in ether. Yield 18.08 g or 95% of the theoretical.

7.350 mg substance: 0.2[illegible] ml N_2 (24°, 732.5 mm). 0.1977 g substance : 5.49 ml 0.1 N $AgNO_3$. Found %
N 3.77; Cl 9.85. $C_{13}H_{22}O_4NBr \cdot HCl$. Calculated % N 3.76; Cl 9.52.

Diethyl ester of quinuclidine-2,2-dicarboxylic acid (V)

18.63 g of 4-(β,β-dicarbethoxy-β-bromoethyl)-piperidine hydrochloride was dissolved in a small amount of water, 20 ml of a 50% potassium carbonate solution added, the separated base extracted with ether, and the extracts dried for a short time with potassium carbonate. The ether solution was then filtered from the potassium carbonate, the ether removed, the residue mixed with 75 ml of pyridine, and solution obtained heated for 2 hours to a weak boil. Pyridine was removed in vacuum, the residue was mixed with 10 ml of a 50% solution of potassium carbonate, the separated oil extracted with ether, and the extract dried with potassium carbonate. After the removal of the ether, the residue was distilled in vacuum. 9.6 g of a colorless oil boiling at 9 mm at 153-155° was obtained. Yield 75% of the theoretical.

The substance possessed a specific odor reminiscent of the odor of piperidine. It was readily soluble in water and the common organic solvents.

3.890 mg substance: 0.196 ml N_2 (22°, 738 mm). Found %: N 5.66. $C_{13}H_{21}O_4N$. Calculated %: N 5.49.

The hydrochloride was an oil; the picrate, yellow prisms (from alcohol) melting at 177-178°.

4.291 mg substance: 7.430 mg CO_2; 1.854 mg H_2O. 2.292 mg substance: 0.233 ml N_2 (19°, 754.5 mm). Found %: C 47.22; H 4.83; N 11.68. $C_{13}H_{21}O_4N \cdot C_6H_3O_7N_3$. Calculated %: C 47.09; H 5.00; N 11.58.

Quinuclidine-2-carboxylic acid

A solution of 8.2 g of the diethyl ester of quinuclidine-2,2-dicarboxylic acid in 80 ml of concentrated hydrochloric acid was heated for 8 hours to a slow boil. Then the hydrochloric acid was vacuum distilled or evaporated on the water bath until the start of crystallization. After cooling, the crystals were filtered, washed with acetone, and dried at 110°. 4 g was obtained. The filtrate was again evaporated until the start of crystallization, diluted with 4 volumes of acetone, and the crystals which separated, filtered. The total yield of quinuclidine carboxylic acid hydrochloride was 6 g or 98% of the theoretical.

For analysis, the substance was dissolved in 95% of alcohol and precipitated from solution with ether. Colorless crystals, melting at 292-294° (with decomposition). Readily soluble in water, poorly in alcohol, and insoluble in acetone.

4.925 mg substance: 9.049 mg CO_2: 3.170 mg H_2O. 0.1208 g substance: 6.22 ml 0.1 N $AgNO_3$. Found %: C 50.11; H 7.20; Cl 18.3. $C_8H_{13}O_2N \cdot HCl$. Calculated %: C 50.11; H 7.36; Cl 18.5.

For the preparation of the free acid, part of the hydrochloride obtained was dissolved in water, mixed with moist silver oxide, shaken for 2 hours, the precipitate filtered, the filtrate treated with hydrogen sulfate, and filtered from the precipitated silver sulfide.

Upon the evaporation of the filtrate, the free quinuclidine carboxylic acid was obtained in the form of a white powder. For purification, the acid was dissolved in chloroform and precipitated from the solution by the addition of dry ether or recrystallized from a mixture of alcohol and acetone.

A white crystalline powder with m.p. 276-278° (with decomposition) (according to literature date [4], the melting point is 280° with decomposition). It is readily soluble in water, alcohol, and chloroform; it is insoluble in acetone and ether; it sublimes in vacuum without decomposition.

7.596 mg substance: 0.589 ml N_2 (19°, 748 mm). Found %: N 8.92. $C_8H_{13}O_2N$. Calculated %: N 9.03.

2-Bromoquinuclidine

2.3 g of the silver salt of quinuclidine-2-carboxylic acid dried in vacuum at 60°, was mixed with 45 ml of dry carbon tetrachloride. 1.4 g of dry bromine was added to the mixture at 0° with efficient stirring, and the mixture heated for 30 minutes at 80°. Upon cooling, of the reaction mixture, the precipitate was filtered and washed with carbon tetrachloride. The filtrate was shaken with a saturated potassium carbonate solution, and then dried with anhydrous potassium carbonate. After the distillation of the carbon tetrachloride, and the removal of its traces in vacuum, 0.27 g of a yellow oil was obtained. The substance was converted to a picrate, and the latter recrystallized from alcohol. A yellow crystalline powder with m.p. 175°. Yield 16% of the theoretical.

4.338 mg substance N_2 (19°, 740 mm). 5.871 mg substance: 2.606 mg AgBr. Found %: N 13.17; Br 18.88. $C_7H_{12}BrN \cdot C_6H_3O_7N_3$. Calculated %: N 13.36; Br 19.09.

Quinuclidine-2-carboxylic amide

A mixture of 4 g of quinuclidine-2-carboxylic acid hydrochloride and 20 ml of pure thionyl chloride was heated for 3 hours at 60-65° (bath temperature). The excess thionyl chloride was removed in vacuum at the same temperature, and absolute benzene twice added to the residue followed by removal in vacuum. A white crystalline residue which was the hydrochloride of quinuclidine carboxylic acid was mixed with cooling with strong ammonia solution. The amide formed was salted out with potassium carbonate and extracted with chloroform.

After the drying of the extract with potassium carbonate and the removal of the chloroform, 2.3 g quinuclidine carboxylic amide, in the form of a white crystalline powder with m.p. 142-143°, was obtained. Yield 72% of the theoretical. The substance was readily soluble in water, alcohol, and chloroform, and almost insoluble in ether and benzene. After recrystallization from a mixture of alcohol and ether, the melting point was unchanged.

3.517 mg substance: 0.573 ml N_2 (18°, 733.5 mm). Found %: N 18.43. $C_8H_{14}ON_2$. Calculated %: N 18.18.

2-Cyanoquinuclidine

1 g of quinuclidine-2-carboxylic amide was heated with 10 ml of thionyl chloride for 4.5 hours at 100° in a sealed tube. The thionyl chloride was then removed in vacuum, the residue mixed with a 50% potassium carbonate solution, and the oil which separated extracted with ether. After drying of the extract with potassium carbonate and the removal of the ether, 0.45 g of a light yellow oil, which was 2-cyanoquinuclidine, was obtained. Yield 51% of the theoretical. The substance is readily soluble in the usual organic solvents, and poorly in water.

The picrate was a yellow crystalline powder (from acetic acid); m.p. 212°.

2.775 mg substance: 4.709 mg CO_2; 1.006 mg H_2O. 2.730 mg substance: 4.620 mg CO_2; 0.990 mg H_2O. 3.282 mg substance: 0.555 ml N_2 (21.5°; 732 mm). Found %: C 46.28, 46.15; H 4.05, 3.96; N 18.90. $C_8H_{12}N_2 \cdot C_6H_3O_7N_3$. Calculated %: C 46.01; H 4.14; N 19.20.

SUMMARY

1. A new method for the synthesis of quinuclidine-2-carboxylic acid was developed, starting with γ-picoline and mesoxalic ester by means of 4-(β,β-dicarbethoxyvinyl)-pyridine, 4-(β,β-dicarbethoxy-β-bromoethyl)-piperidine, and the diethyl ester of quinuclidine-2,2-dicarboxylic acid.

2. The synthesis was accomplished in 5 stages wherein the yield of quinuclidine-2-carboxylic acid as the hydrochloride was 20% of theory based on mesoxalic ester.

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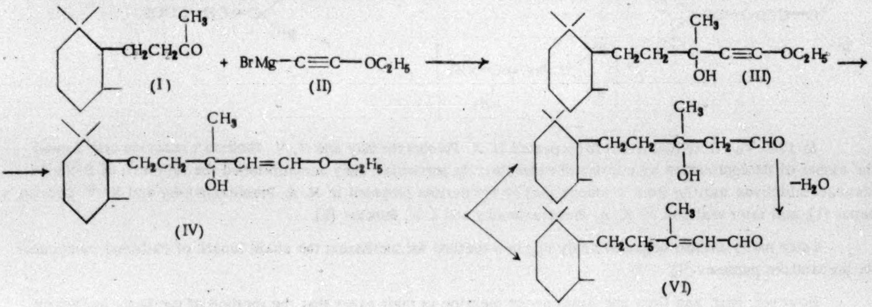
* See Consultants Bureau Translation, page 1379.

ON THE N. A. PREOBRAZHENSKY AND V. V. SHOKINA REACTION

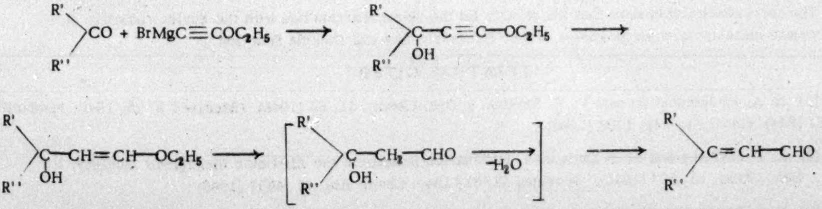
E. I. Genkin

In the past few years, extensive application has been made in the synthesis of organic compounds of the reaction for increasing the chain length of aldehydes and ketones by a =CH–CHO group with the use of ethoxyacetylene magnesium bromide. Soviet chemists N. A. Preobrazhensky and V. V. Shokina [1] first discovered this reaction in 1940, and accomplished the conversion of tetrahydroionone (I) into tetrahydroionylideneacetaldehyde (VI) in the following manner:


CH₃
CH₂CH₂CO
(I)
+ BrMg—C≡C—OC₂H₅
(II)
CH₃
CH₂CH₂—C—C≡C—OC₂H₅
OH (III)
CH₃
CH₂CH₂—C—CH=CH—O—C₂H₅
OH
(IV)
CH₃
CH₂CH₂—C—CH₂—CHO
OH
−H₂O
CH₃
CH₂CH₂—C=CH—CHO
(VI)

The starting substance, which made possible the above synthesis, was ethoxyacetylene, first obtained in 1940 by A. E. Favorsky and M. N. Shchukina [2].

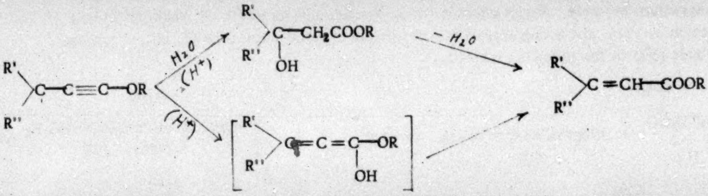
The above synthesis was regarded by the authors as a model for the preparation of β-ionylideneacetaldehyde necessary for the preparation of Vitamin A; the change of the starting tetrahydroionone to β-ionone should lead, according to this scheme to β-ionylideneacetaldehyde [1], which, indeed, was realized later by N. A. Preobrazhensky and I. A. Rubtsov [3]. This discovery, made by N. A. Preobrazhensky and V. V. Shokina, had the following introductory conclusion: "We consider that this reaction is generally applicable for the majority of ketones and aldehydes and opens a new method for the synthesis of unsaturated aldehydes with different radicals at the carbon atom" [1]. Therefore, the Preobrazhensky and Shokina Reaction can be represented in the following general form:


R'
CO + BrMgC≡COC₂H₅
R''
R'
C—C≡C—OC₂H₅
OH
R''
R'
C—CH=CH—OC₂H₅
OH
R''
R'
C—CH₂—CHO
OH
R''
−H₂O
R'
C=CH—CHO
R''

Giving an evaluation of this method for the preparation of β-ionylideneacetaldehyde, B. G. Sasinov and G. S. Tretyakova in one of the reviews [4] correctly point out: N. A. Preobrazhensky's method, proposed in 1945 [1], must be recognized as being the best of the methods reported in the literature for the preparation of β-ionylideneacetaldehyde.

The above paper was first published in the "Journal of General Chemistry" in 1945 (v. 15, No. 1-2, p. 65-69) where in the usual publishers note on the date the paper was received it stated (p 69): "Received September 25, 1940, resubmitted March 16, 1944 ". The initial publication of the paper was held up, apparently, by the start of the Great Patriotic War in 1941. For this reason the paper appeared only in 1945.

The conclusion of the author on the universality of the reaction developed by him was soon confirmed by M. N Shchukina and I. A. Rubtsov [5] who showed, in addition, that ethoxyacetylenylcarbinols formed by the condensation of ethoxyacetylenyl magnesium bromide with carbonyl compounds readily underwent the subsequent transformation: "they are converted into esters of β -hydroxyacids or $\alpha\beta$-unsaturated acids by the action of dilute acids [5]:



In 1947 Van Dorp and Arens [6] repeated N. A. Preobrazhensky and V. V. Shokina's reaction and showed the extent of its application by a series of examples. In particular, they accomplished the synthesis of β-ionylideneacetaldehyde starting from β-ionone [6a] by the outline proposed in N. A. Preobrazhensky and V. V. Shokina's paper [1], and later realized by N. A. Preobrazhensky and I. A. Rubtsov [3].

Later many authors began to apply this new method for increasing the chain length of carbonyl compounds for preparative purposes [7].

However, first, van Dorp and Arens do not mention in their paper that the method of synthesis studied by them was previously proposed by the Soviet chemists N. A. Preobrazhensky and V. V. Shokina; second, the above reaction received the incorrect designation as the "Van Dorp and Arens Reaction," in the foreign periodical chemical literature, in spite of the fact that the priority for this reaction without any doubt lies with the Soviet chemists N. A. Preobrazhensky and V. V. Shokina.

It is necessary to reject the possibility that Van Dorp and Arens as well as authors subsequently using the above reaction had no knowledge of the existence of the paper of N. A. Preobrazhensky and V. V. Shokina, as well as the papers of A. E. Favorsky and M. N. Shchukina, and M. N. Shchukina and I. A. Rubtsov, since the presence of the corresponding references to these papers in "Chemical Abstracts," (see [1-3,5]) excludes this possibility. The paper of N. A Preobrazhensky and V. V. Shokina is also mentioned in the review article by S. T. Ioffe: "The Contribution of Russian Chemists to the Development of the Organo-Magnesium Synthesis, published in the central Soviet chemical journal, "Progress in Chemistry" [8].

The facts conclusively show that the priority for the above reaction lies with the Soviet chemists; it, with complete correctness, must be known as the "Preobrazhensky and Shokina Reaction".

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THE DISTINGUISHED SOVIET SCIENTIST, ILYA ILYICH CHERNYAEV

COMMEMORATION OF HIS SIXTIETH BIRTHDAY)

A. V. Babaeva

The largest school in the world of chemists specializing in inorganic complexes was created in Russia by that talented Russian scientist L. A. Chugaev. Chugaev died young but his students continue the work that he started; they have developed, extended and consolidated the chemistry of complex compounds in the service of the socialist Fatherland.

The outstanding student of L. A. Chugaev is academician Ilya Ilyich Chernyaev, who made many discoveries and carried out many investigations in the field of complex compounds of the platinum metals. He is rightly regarded as one of the creators of refining technology in the Soviet precious metals industry and has tirelessly exerted himself together with his students in furthering its interest. With the name of I. I. Chernyaev is associated the creation of a new and advanced method for purification of platinum, its separation in the highest degree of purity, the preparation of pure osmium, a method for extracting platinum metals from poor ores, the development of a series of analytical methods for the very complicated analysis of noble metals, and the solution of many other critical problems of the industry.

It is difficult to overestimate the fruitful activity of I. I. Chernyaev and his school in the field of refining of platinum and its congeners. The USSR leads the world in the extraction and processing of platinum ores, and the technology of refining of precious metals is the pride of our country. The services of I. I. Chernyaev and his school have been recognized by the Government. It must be stated that their achievments were dependent on the previous extensive and penetrating investigations of the chemistry of complex compounds of the precious metals.

Among the many investigations carried out by Ilya Ilyich, special interest attaches to those on compounds of bi- and quadrivalent platinum containing a nitro group, since these investigations led to his discovery in 1926 of the law of the trans-effect.

The trans-effect law represents an important extension of the coordination theory of the structure of complex compounds, based on the systematic development of the ideas of V. V. Markovnikov about the interaction of the component parts of molecules.

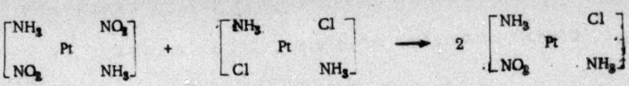
Although paying due respect to the coordination theory, I. I. Chernyaev nevertheless considered that it is too "geometrical" and lacks dynamism. On the basis of this theory, capable as it is of predicting the number of possible geometrical configurations of a molecule, it is impossible to draw any conclusions as to the interaction of the components of the coordination sphere or, in turn, any conclusions about the mode of synthesis of the compounds.

When investigating various platinum compounds containing nitro groups I. I. Chernyaev observed a substitution reaction at the linkage of the central atom with substituents located in the trans-position to the nitro-groups. As a result of the study of diverse reactions of complex compounds of bivalent platinum, I. I. Chernyaev established that the loosening and strengthening of the bond of a given substituent with the central atom depends on the nature of the group or atom present in the trans-position, acidic groups producing a greater trans-action than neutral molecules. Further work in collaboration with A. D. Gelman widened our knowledge of the phenomenon in that it was observed that such unsaturated molecules as ethylene, propylene, nitric oxide and carbon monoxide are characterized by a marked trans-effect in complex compounds. It was therefore inferred that the trans-effect of substituents increases with increased covalence of the bond.

In respect of trans-activity, inner-sphere substituents are arranged in the following approximate order:

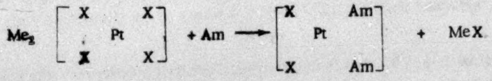
$$R_2S > NO_2 > I > Br > Cl > F > OH > RNH_2 > NH_3 > H_2O$$

Examination by I. I. Chernyaev of inner-sphere reactions of such well-investigated complex compounds as compounds of cobalt and chromium showed that the positions of maximum activity are arranged in the inner sphere in accordance with the principle of the trans-effect. I. I. also explained the exchange reaction of nonelectrolytes, discovered by him, on the basis of the trans-effect:



$$\begin{bmatrix} NH_3 & & NO_2 \\ & Pt & \\ NO_2 & & NH_3 \end{bmatrix} + \begin{bmatrix} NH_3 & & Cl \\ & Pt & \\ Cl & & NH_3 \end{bmatrix} \longrightarrow 2\begin{bmatrix} NH_3 & & Cl \\ & Pt & \\ NO_2 & & NH_3 \end{bmatrix}$$

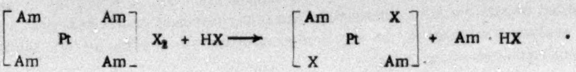
The cis- and trans- forms of platinum compounds can be traced to a single cause on the basis of the trans-effect. Indeed, the formation of cis-diammines from acido complexes by reaction with ammines:



$$Me_2\begin{bmatrix} X & & X \\ & Pt & \\ X & & X \end{bmatrix} + Am \longrightarrow \begin{bmatrix} X & & Am \\ & Pt & \\ X & & Am \end{bmatrix} + MeX$$

(cis-form)

and the formation of trans-diammines from tetrammines by the action of acids:

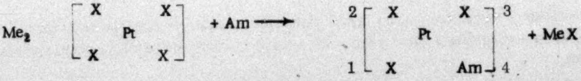


$$\begin{bmatrix} Am & & Am \\ & Pt & \\ Am & & Am \end{bmatrix} X_2 + HX \longrightarrow \begin{bmatrix} Am & & X \\ & Pt & \\ X & & Am \end{bmatrix} + Am \cdot HX$$

(trans-form)

become comprehensible if we take the trans-effect into account.

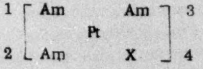
The formation of a cis-diammine $[(AmX)_2\,Pt]$ naturally proceeds through the formation of the monoammine:



$$Me_2\begin{bmatrix} X & & X \\ & Pt & \\ X & & X \end{bmatrix} + Am \longrightarrow \begin{array}{c} 2 \\ \\ 1 \end{array}\begin{bmatrix} X & & X \\ & Pt & \\ X & & Am \end{bmatrix}\begin{array}{c} 3 \\ \\ 4 \end{array} + MeX$$

the acid substituents in positions 1 and 3 in this monoammine being mutually labile, whereas the substituent in position 2 is in a more stable form since it is located opposite to a trans-influencing ammine group. Due to this, the reaction of further substitution by the ammine must proceed at positions 1 or 3, which are completely equivalent, and must lead to a diammine with trans-configuration.

The very first stage in the action of acids on tetrammines of bivalent platinum is the formation of the triammine (A). In this molecule the most labile



$$\begin{array}{c} 1 \\ \\ 2 \end{array}\begin{bmatrix} Am & & Am \\ & Pt & \\ Am & & X \end{bmatrix}\begin{array}{c} 3 \\ \\ 4 \end{array}$$

(A)

ammine is the group in position 1 since it is exposed to the trans-effect of the acid group, and therefore the further action of acid causes substitution of this very ammine and this leads to formation of a trans-ammine. Thus the trans-effect provided a uniform explanation of the long-known empirical cis- and trans-law.

Guided by the discovery of the principle and pursuing the aim of precise determination of the place of reaction of the substituent in the inner sphere of the complex compound, I. I. Chernyaev synthesized triammines with the general formula $[A_1A_2A_3NO_2Pt]X$ He succeeded in obtaining the compound $[Py \cdot NH_3 \cdot NH_2OH \cdot NO_2Pt]X$ in three geometrically isomeric forms.

For the compound $[C_2H_4(NH_2)_2 \cdot NH_3ClBrNO_2Pt]X$ the coordination theory predicts six isomers. The synthesis of these six compounds, if attempted at random, would require an enormous period of time and might not even be successful. I. I. Chernyaev synthesized five out of the six possible geometrical isomers.

I. I. Chernyaev and his pupils carried out a series of investigations of the optical activity of complex compounds of tetravalent platinum arising out of their molecular asymmetry. A series of compounds of these types was resolved into their optical antipodes with the aim of confirming the correctness of the configuration attributed to the tetrammines and triammines of quadrivalent platinum. This was no light task. The actual synthesis of the racemates of these compounds was only possible by utilization of the law of the trans-effect.

Illustrative of the fruitfulness of the application of the trans-effect is the large number of USSR publications on the synthesis of complex compounds of various metals and in particular of complex compounds of metals of the platinum group.

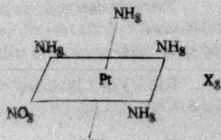
What is the precise physical significance of the phenomenon of the trans-effect? Is it characteristic only of compounds with a coordination structure or has it a more general significance? Is the trans-effect peculiar to compounds in the crystalline state, or is it the consequence of interaction with a solvent, since the trans-effect is almost invariably associated with reactions in solutions and predominantly in water? None of these problems has yet been fully solved.

In the first years following its discovery, the author of the trans-effect explained it on the basis of the Werner hypothesis of "passive resistance" developed in the inner sphere of the complex compound and stabilizing this sphere. According to I. I. Chernyaev, this "passive resistance", possessing not only magnitutude, but also direction is concentrated in that part of the sphere where the acid substituent is most firmly bonded to the central atom, so that the "passive resistance" is diminished in the opposite side of the sphere, i.e. in the trans-position to the acid substituent, with consequent loosening of the bond with the central atom.

A. A. Grinberg and B. V. Nekrasov made almost simultaneous attempts at a physical treatment of the trans-effect. They regard the trans-effect as a special case of counterpolarization, associated in the case of differently characterized and differently polarized substituents with anisotropy of the field of the central atom, creating favorable conditions for lability of the substituent located in the trans-position to the substituent with the highest polarization. There are a series of objections, however, to this treatment, since it makes assumptions that do not always accord with the facts.

At the present time, I. I. Chernyaev regards the trans-effect as an inner-sphere catalysis with the electrons playing a directive part. He attributes the trans-effect to all atoms, molecules and electrons without exception. In complex compounds the central atom also possesses a trans-effect. " The universality of the trans-effect" writes Chernyaev - "requires that the central atom should also possess the same catalytic bond as exists between the atoms of the molecules linked to it".

In compound (B) not only does the nitro group render labile the opposite Pt–NH_3 bond, but the trans-effect of the platinum atom leads to labilization of the N–H bond and to equiponderant detachment of a proton from ammonia and transformation of the ammonia into an amino group:



(B)

$$RNH_3 \rightleftarrows RNH_2^- + H^+ .$$

This phenomenon, observed by Kleve and later by Chugaev in the platinum pentammines, was also observed by Chernyaev in a series of other amino compounds of quadrivalent platinum and in hydroxylamino compounds of bivalent platinum; pupils of I. I. Chernyaev also observed it in acetoxime compounds of bivalent platinum.

The aquo-hydroxo-reactions $[RH_2O \rightleftarrows [ROH + H^+$, which are known not only in the case of complex compounds of metals of the platinum group, but also in that of compounds of chromium and cobalt, must in Chernyaev's opinion be explicable also on the bais of the trans-effect of the central atom. Even if the amino reaction and the hydroxo reaction do not always take place in presence of amines and water in the inner sphere of the complex compound, this can be explained not by the absence of the trans-effect of the central atom, but possibly by the geometrical arrangement of the components of the molecule which is such as to protect the hydrogen of the water and amines against the trans-effect. Also illustrative of the trans-effect of the central atom, in Chernyaev's opinion, is the behavior of the oxygen in the nitro group of complex compounds, for example, in $[(NH_3)_3NO_2Pt]X$. Being subject to the trans-effect of the platinum, it is more labile than the oxygen in the free NO_3^- ion, and that is why the nitro group in complex compounds is also reduced by hydrogen to the amino group, while heating of complex compounds containing a nitro group with ammonium chloride leads to the reaction of N. N. Zinin:

$$RNO_2 + NH_4Cl \longrightarrow RCl + N_2 + H_2O$$

I. I. Chernyaev regards the trans-effect as a general principle which also accounts for the limited magnitudes of the coordination number and the difference in the behavior of the inner-sphere and outer-sphere groups. Concerning the latter, the author of the trans-effect writes: " since the effect of the central atom is to cause weakening of the existing chemical bonds in the combined molecule, this can make all the more impossible the formation of chains from the molecules linked to the central atom".

All this, however, is a long way from revealing the true nature of such a remarkable phenomenon as the trans-effect. " It is only perfectly clear", writes Chernyaev in one of his papers, "that in the field of the chemistry of complex compounds, the principle of the trans-effect is that expression of a unified law of interaction of the atoms constituting a molecule whose clarification for carbon compounds was the dream of V. V. Markovnikov".

For the discovery, expression and application of the law of the trans-effect, I. I. Chernyaev received the Stalin Prize, First Class, in 1952.

Headed by Academician I. I. Chernyaev, the N. S. Kurnakov Institue of General and Inorganic Chemistry of the Academy of Sciences of the USSR has carried out investigations over a wide front on important problems of physicochemical analysis, complex compounds and the chemistry of metals and salts.

Under the direct supervision of I. I. Chernyaev, the Platinum Section, apart from chemical investigations of complex compounds, is studying their physicochemical and physical properties: electric, magnetic, spectral, crystal-chemical, thermochemical, etc., a knowledge of which is necessary for clarification of the nature of the trans-effect and its quantitative characterization. The application of a dominating idea in these investigations is an advantage to the Soviet school of complex chemistry which is not shared by foreign workers.

Investigators who are working on the above-mentioned problems of complex compounds in the laboratories of the Institute of General and Inorganic Chemistry of the Academy of Sciences of the USSR are also solving important practical problems in collaboration with industry.

Twenty years ago, at the session of the Academy of Sciences of the USSR devoted to problems of the Ural-Kuzbas, I. I. Chernyaev said: " We must hope that the fusion of theory and practice in the future will lead us to mastery over materials on a scale undreamed by the greatest enthusiasts "

Ilya Ilyich Chernyaev realized this fusion of theory and practice throughout the whole of his scientific activity and his activity as director of the institute.

Received January 5, 1953.

THE THERMOCHEMISTRY OF CUPRAMMONIUM COMPLEXES IN AQUEOUS SOLUTION

K. B. Yatsimirsk[illegible] and Z. M. Grafova

The cuprammonium complex compounds have been the subject of many investigations. These compounds as we know, find extensive practical application. Many workers have studied the equilibria in aqueous solutions of cuprammonium complexes [1, 2, 3,]. These studies have revealed the composition of cuprammonium complexes, have demonstrated the stepwise character of the complex-formation, and have enabled calculation of the instability constants of a series of ions of the type of $Cu(NH_3)_n^{2+}$ (n = 1, 2, 3, 4, 5).

In respect to their thermochemistry, these complex compounds have clearly not been adequately investtigated.

About 50 years ago, Bouzat [4] determined the heats of mixing of aqueous solutions of ammonia and copper sulfate. Experiments were performed at temperatures of 10-13 °C; the data obtained relate to a narrow range of ammonia concentrations (0.5 to 1M).

Quite recently, Fyfe [5] determined the heat of mixing of a 1 M solution of amonia with a copper salt solution at temperatures of 14-17° and obtained a value close to that found by Bouzat.

It may be pointed out that Fyfe erroneously regards this value as the heat of formation of $Cu(NH_3)_4^{2+}$ from the copper ion and aqueous ammonia. Actually a 1 M solution of ammonia only contains 77% of the copper in the form of $Cu(NH_3)_4^{2+}$ [6], the remaining 23% being in the form of $Cu(NH_3)_3^{2+}$.

Data for more concentrated solutions of ammonia are lacking in the literature. There are no data that permit evaluation of the possibility of formation of mixed complexes of the type of $[Cu(NH_3)_n(OH)_m]^{2-m}$. However, the probability of formation of such complexes is extremely high, since complex ions of the type of $Cu(NH_3)_4^{2+}$ and $Cu(OH)_4^{2-}$ are distinguished by great stability [7].

EXPERIMENTAL

The previously described apparatus and procedure [8] were used for determination of the heats of mixing of a solution of copper sulfate with solutions of ammonia, and also of solutions of cuprammonium complexes with solutions of caustic alkali.

In the first series of experiments the calorimeter was filled with solutions of ammonia of various concentrations (from 0.5 to 6.9 M). One and the same volume of ammonia solution (500 ± 1 ml) was used in all the experiments. The weight of the test solutions was determined on a technical balance.

A 0.304 M copper sulfate solution (the copper content of the solution was determined by the electrogravimetric method) was poured into glass ampoules with a small glass side bulb (the weight of copper sulfate was determined on an analytical balance) The ampoule was then introduced into the calorimetric liquid and crushed against the side wall of the Dewar vessel after establishment of a uniform temperature gradient. In view of the fact that the duration of the main period did not exceed 3-4 minutes, the radiation correction was found by a graphical method. The water number of the calorimeter was found from the heat of solution of a definite weight of chemically pure potassium chloride and was 65 ± 0.5 cal/g.

The heat capacity of aqueous solutions of ammonia has been determined by Vrevsky and Kaigorodov [9] who found that over the whole range of concentrations the heat capacity is equal to unity with insignificant variations in the third decimal place. The values of Vrevsky and Kaigorodov were subsequently confirmed [10].

Introduction into the solution of minute amounts of a copper salt (the concentrations of $Cu(NH_3)_n^{2+}$ did not exceed 0.004 M) could not appreciably change the heat capacity of the solution, and therefore we assumed in all cases that the heat capacity of the prepared solutions was unity. The deviation between parallel experiments did not exceed ± 3%. A summary of the results obtained is given in Table 1.

TABLE 1

Heat of mixing of solutions of copper sulfate with solutions of ammonia

Prep. No.	Ammonia conc (moles/l.)	Amt. of copper (g)	Temp. change with radiation correction	Radiation correction	Heat capacity of calorimeter (in kcal)	Heat of mixing (in kcal per mole Cu)	Mean value of Δ H (in kcal)
1	0.5	0.1342	0.0676	0.0016	565.9	18.5	−18.5
2	1.0	0.1149	0.0662	0.0009	561.4	21.0	−20.7
		0.1328	0.0732	0.0028	562.7	20.4	
3	2.0	0.1290	0.0826	0.0005	560.9	23.4	−23.3
		0.1146	0.0736	0.0010	557.2	23.2	
4	3.8	0.1216	0.0894	0.0005	552.5	26.5	−26.8
		0.1294	0.0992	0.0014	552.7	27.1	
5	4.9	0.1075	0.0846	0.0015	550.6	28.0	−28.0
6	6.9	0.1442	0.1232	0.0048	542.2	30.1	−30.2
		0.1342	0.1174	0.0057	540.8	30.6	
		0.1051	0.0908	0.0030	539.3	30.1	

In a second series of experiments the calorimetric liquid was a solution of a cupramonium complex in ammonia. The initial concentration of ammonia in all cases was 0.68 M, but the concentration of the cuprammonium complex was varied from 0.00160 to 0.00573 M. A 4 N solution of NaCH was poured into ampoules.

The weight of the NaOH solution was determined on an analytical balance. After a uniform temperature gradient had been established the ampoule was crushed. All measurements and calculations were performed as in the first series of experiments.

In preliminary experiments it was established that on crushing an ampoule containing alkali solution in 0.68 M ammonia, no temperature change was observed, and therefore the absorption of heat is bound up with reaction between the cuprammonium complex and the alkali. Experimental results are set out in Table 2.

EVALUATION OF RESULTS

The heats of mixing of solutions of copper salts and ammonia at relatively low concentration of ammonia (0.5-1.2 M) were determined by Bouzat [4] and us. The values that we obtained, notwithstanding the different experimental temperature, substantially agreed with those of Bouzat. With increasing ammonia concentration, the heats of mixing rise very considerably.

On comparing the results with our data for nickel salts, we see that at low ammonia concentrations the heats of formation of cuprammonium complexes in aqueous solution only slightly exceed in absolute value the heats of formation of nickel-ammonium complexes [8].

Sharp differences in heats of mixing are observed at high ammonia concentrations (see diagram). In the case of formation of cuprammonium complexes, the value of the heat of mixing does not tend to approach any definite value, but continuously rises. This course of the curve may be explained by the fact that side by side with the $Cu(NH_3)_4^{2+}$ complex there is formed in solution the complex ion of $Cu(NH_3)_5^{2+}$ which is not characterized by special stability.

TABLE 2

Heats of Mixing of Solutions of Cuprammonium Complex with Alkali Solution

No. of expt.	Wt. of solution (g)	Concentration of cuprammonium complex in solution (moles/liter)	Temp. change with correction for radiation.	Correction for radiation	Heat capacity of calorimeter (cal)	Heat of mixing (kcal/mole)	Mean value of ΔH
1	5.7816	0.00160	−0.0070	0.0009	558.3	− 3.08	
2	5.7934	0.00305	−0.0122	0.0002	558.3	− 2.93	+ 3.03
3	5.7952	0.00573	−0.0121	0.0009	559.3	− 3.00	

According to Bjerrum the equilibrium constant of the reaction $Cu(NH_3)_5^{2+} \rightleftharpoons Cu(NH_3)_4^{2+} + NH_3$ is 0.3. Consequently even in 7 M ammonia solution there is present 32% $Cu(NH_3)_4^{2+}$ and 68% $Cu(NH_3)_5^{2+}$.

Another conspicuous feature is the marked difference between the heats of formation (from the copper ion and ammonia in aqueous solution) of the complex ions of $Cu(NH_3)_4^{2+}$ and $Cu(NH_3)_5^{2+}$. Whereas for the former ion $\Delta H > -19$ kcal, for the second it is < -30 kcal. Addition of the fifth molecule of ammonia to the tetrammine complex is accompanied by an extremely large thermal effect ($\Delta H < 11$ kcal). There is no parallelism between the successive heats of addition of molecules of ammonia and the change of standard thermodynamic potential. Furthermore, an inverse dependence is observed in the formation of ammoniacal complexes of copper and nickel; the relative stability of the successively formed complexes diminishes, but the successive heats of addition of ammonia molecules rise in absolute value.

Consequently, the change of entropy with successive addition of ammonia molecules does not remain constant but continuously diminishes.

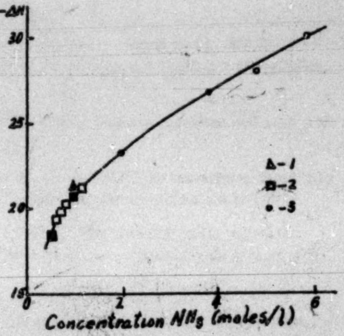


Diagram: Heats of mixing of solutions of copper salts and ammonia. 1. Fyfe's data; 2. Bouzat's data; 3. our data.

The occurrence of a considerable thermal effect during mixing of solutions of caustic alkali with solutions of a cuprammonium complex is evidence, in our opinion, of a reaction in the system which leads to formation of a mixed hydroxo-ammono- complex. The value of the heat of mixing remains constant with changing concentration of cuprammonium complex. Formation of the mixed hydroxo-ammono- complex is accompanied by absorption of heat and, consequently, by an increase of entropy.

SUMMARY

1. The heats of mixing of solutions of $CuSO_4$ with ammonia solutions were determined over a wide range of concentrations (from 0.5 to 6.9 M).

2. The heat of mixing of solutions of NaOH with solutions of cuprammonium complex (0.0016 to 0.0057 M) were determined.

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* See Consultants Bureau English Translation, p. 1765.

PHYSICOCHEMICAL ANALYSIS OF THE BINARY SYSTEMS OF UREA AND ALIPHATIC ACIDS

N. Z. Rudenko and D. E. Dionisyev

The aim of the present investigation was the clarification of the nature of the reaction between urea and acetic, butyric and chloroacetic acids in the liquid phase. The choice of components was dictated by the desire to determine the effect of chain length and of introduction of electronegative substituents on the character of the reaction with urea. Moreover, a study of systems of urea with aliphatic acids is interesting in that urea is one of the most important products of nitrogen metabolism in the animal organism, and in that during digestion the fats are broken down into their components, the fatty acids undergoing further breakdown with formation of lower acids.

We studied the density, viscosity and electric conductivity at three temperatures. The procedure was as previously described [1].

The viscosity was expressed in centipoises, the concentration in mole-%.

The system urea-acetic acid has been often investigated by the fusibility method [2-5]. All the investigators quite definitely established the presence in the system of the compound $CO(NH_2)_2 \cdot 2CH_3COOH$, which dissociates considerably even at the melting point.

The acetic acid used in this work had m.p. 16.6° after purification by freezing; the urea had m.p. 132.7° after repeated crystallization from water.

Viscosity, density and electric conductivity were studied at 80, 90, and 100°. In the system containing more than 70 mole-% urea, appreciable decomposition with loss of carbon dioxide occurred even at 100°.

In Fig. 1 is plotted the dependence of viscosity on concentration. The viscosity isotherms of the system are curves slightly convex to the axis of concentration. The dependence of viscosity on temperature decreases with increasing concentration of acetic acid.

The curves of density versus concentration (Figure 2) are slightly convex to the axis of composition.

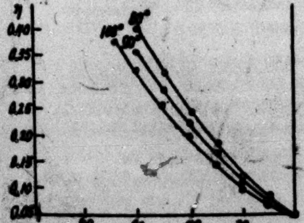

Fig. 1 Viscosity of the system urea-acetic acid.

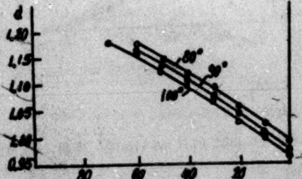

Fig. 2. Specific gravity of the system urea-acetic acid.

Fig. 3 contains plots of electric conductivity (corrected for density) versus composition. These curves are similar to those of the specific electric conductivity, except that they are more convex to the axis of concentration.

We only give the isotherms of electroconductivity corrected for viscosity (ηκ) on the assumption that, with all their defects, such isotherms are more reliable criteria of the processes taking place in the system than specific electric conductivity curves.

System urea-butyric acid has been studied by the fusion method by A. G. Bergman and M. N. Kuznetsova [5]. They established the absence of chemical reaction.

Chemically pure butyric acid was used. It was dried for a long period over anhydrous copper sulfate and then distilled three times with a dephlegmator. B. p. 197.6° at 764 mm.

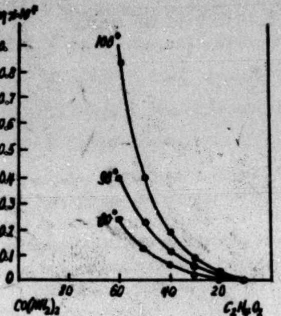

Fig. 3. $\eta\kappa$ of the system urea-acetic acid.

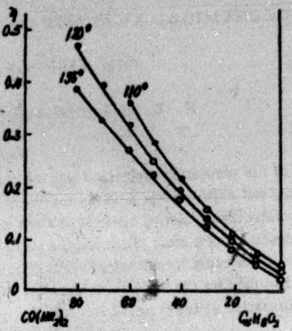

Fig. 4. Viscosity of the system urea-butyric acid.

The viscosity, density and electric conductivity were measured at temperatures of 110, 120, and 135°. Mixtures containing more than 80 mole-% urea decomposed even at 120° with evolution of carbon dioxide.

In Figure 4 is plotted the dependence of viscosity on concentration of components. The viscosity isotherms are slightly convex to the axis of composition.

The density isotherms are almost rectilinear. Rising temperature very slightly reduces the density of the system, and the numerical values for 110, 120 and 135° are very close. For this reason only the 135° isotherm is plotted in Figure 5.

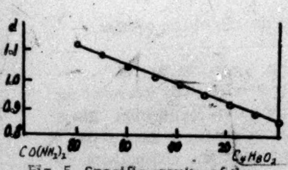

Fig. 5. Specific gravity of the system urea-butyric acid at 135°.

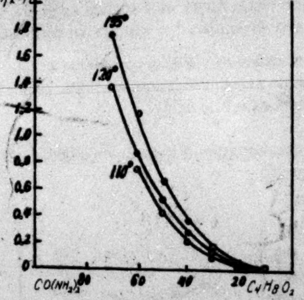

Fig. 6. $\eta\kappa$ of the system urea-butyric acid.

The isotherms of electric conductivity, corrected for viscosity, are curves convex to the axis of composition. The electric conductivity at first rises slowly to 40 mole-% urea and then rapidly with increasing concentration of the latter. The dependence of $\eta\kappa$ on composition is plotted in Figure 6.

The system urea-chloroacetic acid has been studied by the fusion method by Paschin and Rikowski [3] who established the presence of a considerable amount of the dissociated compound $CO(NH_2)_2 \cdot 2CH_2ClCOOH$.

Thrice-distilled, chemically pure chloroacetic acid was used. Fractions with b. p. 187° at 729 mm were collected in ampoules.

Viscosity, density and electric conductivity were measured at temperatures of 80, 90, and 100°. Mixtures containing more than 80 mole-% urea decomposed when heated at above 100°.

The viscosity isotherms shown in Figure 7 are curves convex to the axis of composition. The deviation from additivity is greatest for the 90° isotherm. With rising urea concentration, the temperature coefficient of viscosity increases.

The density/concentration curves are extremely convex to the axis of composition (Fig. 8).

In Figure 9 is plotted the dependence of the electric conductivity, corrected for viscosity, on the concentration. In view of the very close numerical values for temperatures of 80, 90, and 100°, the diagram only gives the 100° isotherm; this is a steadily descending curve with convexity to the axis of composition.

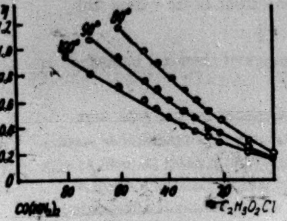

Fig. 7. Viscosity of the system urea-chloroacetic acid.

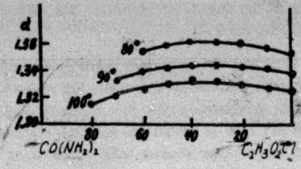

Fig. 8. Specific gravity of the system urea-chloroacetic acid.

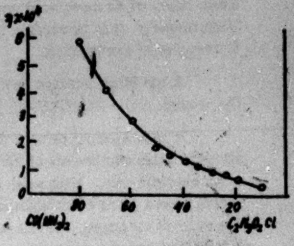

Fig. 9. ηϰ of the system urea-chloroacetic acid, at 100°.

In this system the electric conductivity changed considerably in the course of time while the viscosity and density of the mixtures remained constant. It is characteristic that the electric conductivity changed in the upward direction only in the fused state. We kept mixtures at room temperature in hermetically sealed vessels for over a month and the electric conductivity remained constant. But when the mixtures were fused, the electric conductivity increased at the mean rate of 2% in 15 minutes. The above values of electric conductivity were determined on freshly prepared mixtures after keeping for 15 minutes in a thermostat.

EVALUATION OF RESULTS

In the system urea-acetic acid the viscosity isotherms are curves which are convex to the composition axis and thus indicate dissociation of an associated component. The electrical conductivity curves likewise do not indicate chemical interaction in the system. The density isotherms (curves convex to the composition axis) point to a slight contraction in the system. Dolezalek [6] is of the opinion that such curves indicate chemical reaction. E. B. Viron [7], however, has established that contraction in a system need not be associated with chemical reaction; he showed that isotherms convex to the composition axis may also occur in the absence of chemical reaction. Hence it follows that the density isotherms must be regarded only against the background of other, more significant, properties.

It may be thought that the compound $CO(NH_2)_2 \cdot 2CH_3COOH$, already strongly dissociated at the melting point, would be wholly dissociated in the liquid phase (at 80, 90, and 100°).

Lengthening of the chain in the acid ought not to increase the tendency toward chemical reaction, as was confirmed for the system urea-butyric acid when this was studied in the liquid phase. The isotherms of viscosity and "converted" electric conductivity, convex to the composition axis, do not point to chemical reaction in the system.

We know that the introduction of chlorine into acetic acid increases its acidity, and this ought to promote its reaction with urea.

However, examination of the isotherms of the properties studied in the liquid phase do not give a direct indication of chemical interaction in the system. It may be thought that the compound $CO(NH_2)_2 \cdot 2CH_2ClCOOH$, also strongly dissociated at the melting point, would be fully dissociated in the liquid phase (at the experimental temperatures of 80, 90, and 100°).

According to the generally accepted interpretation, the viscosity isotherms (convex to the composition axis) reflect dissociation of an associated component in the system. With rising temperature, such curves are diminished in convexity and tend to become straight lines. In the system in question the 90° isotherm exhibits the greatest deviation from additivity. It is possible that this abnormality may be provoked by the complexity of the processes taking place in the system and that is is bound up with dissociation of an associated component and the formation of a compound. In that event, with rising temperature there should be found on the viscosity isotherms an indication of chemical reaction on condition that the fall in viscosity of the mixture caused by dissociation of an associated component with rising temperature is not offset by its increase due to reaction. Unfortunately, it is impossible to check this hypothesis due to intensified decomposition in the system with further rise of temperature.

A too large positive deviation of the density isotherms is, in a way, evidence of chemical interaction in the system.

It is interesting to note that urea with strong inorganic acids gives compounds of the 1:1 type, with bivalent acids compounds of the 1:2 type (2 molecules of urea), and in both cases the urea functions as donor of an electron pair. With weak organic monobasic acids, such as acetic and chloroacetic acids (as well as with phenol), urea gives compounds of the 2:1 type (2 molecules of acid), and should thus function as a donor of two pairs of electrons, but this is very improbable because with inorganic acids urea functions as a monoamine. It is noteworthy that urea gives compounds of the latter type with strongly associated components. It is more probable that also in these compounds the urea functions as a donor of only one electron pair but the pair is accepted by a dimer of the second component. Such a compound will, of course, not be distinguished by great stability, and will decompose with rising temperature. It is conceivable that for this very reason compounds of the 2:1 type are not reflected on the isotherms of properties in the liquid phase of both systems with fatty acids and systems with phenol [1].

SUMMARY

1. Determinations were made of the viscosity, density and electric conductivity of the systems urea-acetic acid, urea-chloroacetic acid at temperatures of 80, 90, and 100°, and urea-butyric acid at 110, 120, and 135°.

2. In all three systems no chemical reaction was detected in the liquid phase.

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*See Consultants Bureau Translation, pages 59 ff.

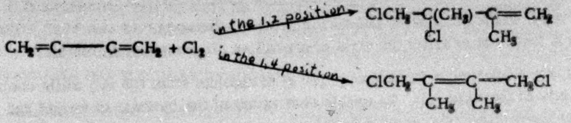
SYNTHESIS OF HYDROCARBONS

XXXIX. 2,3-DIMETHYL–1,3-BUTADIENE DICHLORIDE IN THE SYNTHESIS OF ISOALKENES WITH A CENTRAL DOUBLE BOND

R. Ya. Levina, V. R. Skvarchenko, A. S. Okunevich and E. G. Treshchova

In continuation of our study of the synthesis of olefinic hydrocarbons containing a central double bond by the reaction of dichlorides of conjugated dienes with organomagnesium compounds [1,2,3], we have studied in the present paper the reaction between the dichloride of 2,3-dimethyl-1,3-butadiene (diisopropenyl) and organomagnesium compounds (methyl and propyl magnesium bromides).

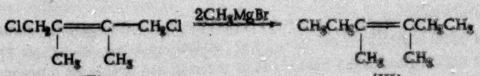
The chlorination of 2,3-dimethyl-1,3-butadiene (here studied for the first time), led to formation of a crystalline dichloride (m.p 35°), apparently the 1,4-dichloride (II), judging by the analogy with the crystalline 1,4-dibromide of butadiene (bromination of butadiene is known to yield a crystalline 1,4 dibromide and a liquid 1,2-dibromide). The crystalline dichloride could, however be contaminated with the 1,2-dichloride (I) of 2,3-dimethyl-1,3-butadiene:



$$CH_2{=}C{-}C{=}CH_2 + Cl_2 \xrightarrow{\text{in the 1,2 position}} ClCH_2{-}\underset{Cl}{C}(CH_3){-}\underset{CH_3}{C}{=}CH_2 \quad (I)$$

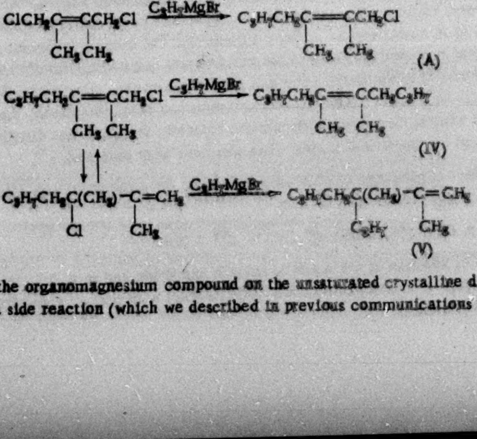
$$\xrightarrow{\text{in the 1,4 position}} ClCH_2{-}\underset{CH_3}{C}{=}\underset{CH_3}{C}{-}CH_2Cl \quad (II)$$

Reaction of crystalline diisopropenyl dichloride with methyl magnesium bromide led to formation of 3,4-dimethylhexene-3 (III) (yield 23% of the theoretical) whose structure was confirmed by analysis, by the constants, and by the Raman spectra:



$$\underset{(II)}{ClCH_2\underset{CH_3}{C}{=}\underset{CH_3}{C}{-}CH_2Cl} \xrightarrow{2CH_3MgBr} \underset{(III)}{CH_3CH_2\underset{CH_3}{C}{=}\underset{CH_3}{C}CH_2CH_3}$$

Reaction of the crystalline diisopropenyl dichloride with propyl magnesium bromide gave a mixture of two hydrocarbons (yield 11% of the theoretical): 5,6-dimethyldecene-5 (IV) (90% of the total) and the isomeric α-olefinic hydrocarbon (V) (10 %), the latter being due to allylic rearrangement of an unsaturated monochloride – the intermediate product (A):



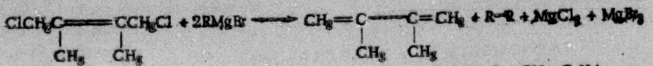
$$ClCH_2\underset{CH_3}{C}{=}\underset{CH_3}{C}CH_2Cl \xrightarrow{C_3H_7MgBr} C_3H_7CH_2\underset{CH_3}{C}{=}\underset{CH_3}{C}CH_2Cl \quad (A)$$

$$C_3H_7CH_2\underset{CH_3}{C}{=}\underset{CH_3}{C}CH_2Cl \xrightarrow{C_3H_7MgBr} C_3H_7CH_2\underset{CH_3}{C}{=}\underset{CH_3}{C}CH_2C_3H_7 \quad (IV)$$

$$\downarrow\uparrow$$

$$C_3H_7CH_2\underset{Cl}{C}(CH_3){-}\underset{CH_3}{C}{=}CH_2 \xrightarrow{C_3H_7MgBr} C_3H_7CH_2\underset{C_3H_7}{C}(CH_3){-}\underset{CH_3}{C}{=}CH_2 \quad (V)$$

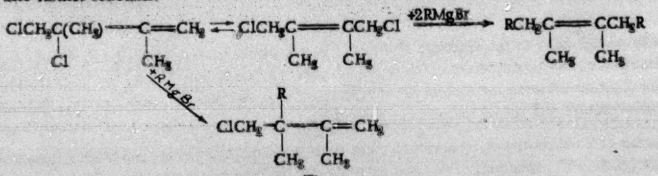
The action of the organomagnesium compound on the unsaturated crystalline diisopropenyl dichloride was also accompanied by a side reaction (which we described in previous communications [1,2,3]) leading to recovery of the original 2,3-dimethyl-1,3-butadiene, while in the case of propyl magnesium bromide, n-hexane was also obtained:



$$Cl\underset{\textstyle CH_3}{CH_2C}=\underset{\textstyle CH_3}{C}CH_2Cl + 2RMgBr \longrightarrow CH_2=\underset{\textstyle CH_3}{C}-\underset{\textstyle CH_3}{C}=CH_2 + R-R + MgCl_2 + MgBr_2$$

(where R = CH_3, C_3H_7)

Possible contamination of the prepared crystalline 2,3-dimethyl-1,3-butadiene dichloride with 1,2-dichloride need not interfere in the reaction with organomagnesium compounds since during the reaction the 1,2-dichlorides either undergo allylic rearrangement to 1,4-dichlorides [1] (which react further with the organomagnesium compound) or exchange only one atom of chlorine per radical and form the monochloride (B) which does not enter into further reaction:



(B)

EXPERIMENTAL

1. Chlorination of 2,3-Dimethyl-1,3-butadiene (Diisopropenyl)

Chlorination of diisopropenyl was performed at various temperatures (between −15 and −75°). The fall in temperature during cooling is found not to affect the yield of crystalline diisopropenyl dichloride.

Chlorine was introduced into a solution of diisopropenyl (20 g) in absolute ether (25 ml) while cooling the reaction vessel with a mixture of snow and salt. To enable observation of the increase in weight and to determine the completion of the reaction, the reaction vessel was counterbalanced on a balance. The reaction was judged complete when the weight of reaction mixture had increased by the theoretical amount, on the basis of the addition of two atoms of chlorine to the diisopropenyl molecule. The required weight increase of 17 g (for 20 g diisopropenyl) was reached after 30-40 minutes.

After distillation of the ether and fractional distillation of the residue in vacuum (from a flask with a tall dephlegmator), the dichloride of diisopropenyl was isolated with b.p. 80-84° (at 18 mm). Almost the whole of the dichloride crystallized when cooled; after pressing and drying on a porous plate, the crystals had m.p. 35°. Yield of crystalline dichloride 32% of the theoretical (300 g diisopropenyl gave 173 g dichloride).

2. Reaction of Crystalline Diisopropenyl Dichloride with Methyl Magnesium Bromide

To methyl magnesium bromide (120 g methyl bromide, 24 g magnesium and 300 ml absolute ether) was gradually added, with water cooling and continuous stirring, a solution of the crystalline diisopropenyl dichloride with m.p. 35° (39 g) in absolute ether at such a speed that the ether only boiled gently. After the whole of the dichloride had been added, the reaction mixture was left overnight. On the next day the stirring was continued for 6 hours at room temperature and for 2 hours on the water bath. Decomposition was effected with dilute acetic acid (10%). After two experiments had been completed, the ether extracts were combined, washed until neutral, and dried with calcium chloride; the ether was distilled off and the residue distilled in a column of 50 theoretical plates. Two fractions were obtained.

The first fraction (product of cleavage of chlorine atoms from the dichloride) was diisopropenyl with b.p. 68.5-69.5° (753 mm); n_D^{20} 1.4380; d_4^{20} 0.7260.

Literature data [4]: b.p. 68.6° (762 mm); n_D^{20} 1.4390; d_4^{20} 0.7262.

The crystalline product of addition of the diene to maleic anhydride had m.p. 79° (from ligroine), in agreement with the literature [5]. A mixed melting test of this adduct with that obtained from the original diisopropenyl did not give a depression.

The yield of diisopropenyl was 15 g or 40% of the theoretical calculated on the initial dichloride.

The second fraction (product of substitution of two atoms of chlorine in the dichloride by methyl groups) had b.p. 119-119.5° (765 mm); yield 13.5 g or 23% of the theoretical (calculated on the initial dichloride).

The second fraction was heated with maleic anhydride in order to eliminate any diisopropenyl and then distilled over sodium in the same column, giving 3,4-dimethylhexene-3 (III), not previously described in the literature. Its constants were:

B.p. 119.2-119.4° (770 mm); n_D^{20} 1.4275; d_4^{20} 0.7415; MR_D 38.89. $C_8H_{16}F$. Calculated: MR_D 38.67.

5.660 mg substance: 17.813 mg CO_2; 7.129 mg H_2O. Found %: C 85.88; H 14.09. C_8H_{16}. Calculated %: C 85.72; H 14.28.

The Raman spectrum of 3,4-dimethylhexene-3 contained the following frequencies (the intensity of the lines was evaluated visually)*:

245 (1; w); 313 (0); 409 (3; w); 421 (0.5); 455 (0.8); 480 (2); 519 (1); 555 (0.5); 585 (2); 600 (1.5); 679 (10); 746 (0); 790 (0.5; w); 846 (1.5); 907 (0); 912 (0); 938 (3.5); 970 (1); 998 (4.5); 1018 (1); 1056 (2.5); 1074 (5); 1101 (1.2; h); 1144 (1; h); 1170 (1.5); 1196 (1.8); 1206 (0); 1237 (1.5); 1268 (2); 1322 (5); 1380 (5); 1440 (2); 1449 (10); 1640 (0.5); 1664 (20).

The presence in the spectrum of a weak frequency of 1640 cm^{-1} points to the presence of traces of an α-olefinic hydrocarbon in 3,4-dimethylhexene-3.

It is noteworthy that whereas for tetramethylethylene (the first member of the series of tetrasubstituted olefins) the characteristic frequency is 1676 cm^{-1} [7], the Raman spectrum of the 3,4-dimethylhexene-3 synthesized by us — also a tetrasubstituted olefin — contains a frequency of 1664 cm^{-1} i.e., lower than that of tetramethylethylene.

3. Reaction of Crystalline Diisopropenyl Dichloride with Propyl Magnesium Bromide

Reaction of propyl magnesium bromide (123 g propyl bromide, 24 g magnesium and 300 ml absolute ether) with diisopropenyl dichloride (m.p. 35°; 47.5 g) was effected in the same conditions as described above for the reaction with methyl magnesium bromide. After two experiments had been carried out, the ether extracts were combined and worked up in the usual manner; the residue was distilled over sodium in a column with 30 theoretical plates. Two fractions were obtained.

The first fraction with b.p. 65-80° (21 g) was a mixture of diisopropenyl and hexane formed by the side reaction of cleavage of chlorine from the chloride. For removal of the formed diisopropenyl and separation of the n-hexane in the pure form, fraction 1 was heated with maleic anhydride and then distilled over sodium in a column of 50 theoretical plates. In all, 9 g of hexane (17% of the theoretical calculated on the diisopropenyl dichloride) was isolated. Its constants were:

B.p. 68.5° (755 mm); n_D^{20} 1.3753; d_4^{20} 0.6584; MR_D 30.0; calculated 29.90.

Literature data [6]: B.p. 68.3 (760 mm); n_D^{20} 1.3751; d_4^{20} 0.6592.

The second fraction was 5,6-dimethyldecene-5 (IV) with b.p. 200-202°; yield 12g (11% of the theoretical). After a second distillation in the same column, the hydrocarbon was free from traces of halogen and had the following constants:

B.p. 201.1-201.2° (751 mm); n_D^{20} 1.4440; d_4^{20} 0.7782; MR_D 57.45. $C_{12}H_{24}F$. Calculated: MR_D 57.15.

5.607 mg substance: 17.840 mg CO_2; 7.210 mg H_2O. 4.300 mg substance: 13.520 mg CO_2; 5.490 mg H_2O. Found %: C 85.87, 85.80; H 14.23, 14.29. $C_{12}H_{24}$. Calculated %: C 85.72; H 14.28. 5,6-Dimethyldecene-5 has not been described in the literature.

The Raman spectrum of 5,6-dimethyldecene-5 contained the following frequencies (intensities evaluated visually).

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* The Raman spectra were plotted in the previously described conditions [1,2].

276 (1); 333 (0.8); 397 (0.5); 410 (1); 491 (1); 522 (1); 586 (1.5); 603 (0.5); 671 (0.5); 695 (1.5); 735 (0.5); 750 (1); 792 (1); 821 (2.5); 845 (0.5); 873 (3); 895 (4); 925 (1); 956 (1); 999 (1); 1050 (4); 1058 (1); 1085 (1); 1102 (4); 1133 (0.5); 1170 (0.5); 1198 (1.5); 1241 (1;h); 1290 (1.5); 1301 (2.5); 1329 (1.5); 1382 (3); 1408 (1); 1443 (10;w); 1459 (3); 1640 (1.5); 1665 (12).

Judging by the Raman spectrum, 5,6-dimethyldecene-5 contained about 10% of an α-olefinic hydrocarbon. Formation of the latter may be explained by allylic rearrangement of an intermediate product of reaction — the unsaturated monochloride (see scheme above).

Consequently, in its reaction with propyl magnesium bromide, diisopropenyl dichloride (II) behaves similarly to butadiene 1,4-dichloride, whose reaction with butyl magnesium bromide also leads to formation of an α-olefinic hydrocarbon isomeric with the main reaction product — an alkene with a central double bond [3].

The spectrum of 5,6-dimethyldecene-5, like that of 3,4-dimethylhexene-3, contains a characteristic frequency of 1665 cm^{-1}, whose value is lower than for tetramethylethylene.

SUMMARY

1. Reaction of the crystalline dichloride of diisopropenyl (2,3-dimethylbutadiene-1,3) with methyl magnesium bromide gave 3,4-dimethylhexene-3 in 23% of the theoretical yield, not previously described in the literature; the hydrocarbon has a branched structure and a central double bond. 3,4-Dimethylhexene-3 was characterized by its constants and its Raman spectrum.

2. Reaction of crystalline diisopropenyl dichloride with propyl magnesium bromide gave a mixture of two hydrocarbons (11% yield): 5,6-dimethyldecene-5 (90%) and an isomeric α-olefinic hydrocarbon (10%) formed by allylic rearrangement of an intermediate reaction product — an unsaturated monochloride.

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Moscow State University

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SYNTHESIS OF HYDROCARBONS

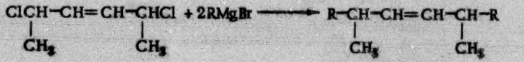
XL. REACTION OF CYCLOPENTADIENE DICHLORIDE WITH ORGANOMAGNESIUM COMPOUNDS

R. Ya. Levina, T. I. Tantsyreva and E. G. Treshchova

The reaction of organomagnesium compounds with unsaturated 1,4-dihalides of the allyl type, studied in previous papers by one of us [1-4], was developed as a new method of synthesis of difficultly accessible olefinic hydrocarbons (trans-form) with normal and iso structures and containing a central double bond.

$$ClCH_2-CH=CH-CH_2Cl + 2RMgBr \longrightarrow R-CH_2-CH=CH-CH_2-R$$

($R = CH_3, C_3H_7, C_4H_9$)



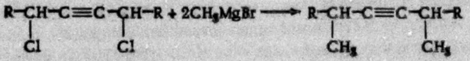
$$\underset{CH_3}{ClCH}-CH=CH-\underset{CH_3}{CHCl} + 2RMgBr \longrightarrow R-\underset{CH_3}{CH}-CH=CH-\underset{CH_3}{CH}-R$$

($R = CH_3, C_2H_5$)

A similar type of reaction, applied to 1,4-dichlorides of the propargyl type (containing a triple bond), served as a method of synthesis of symmetrical dialkyl acetylenes with normal [5,6] and iso structures [7,8]:

$$ClCH_2-C\equiv C-CH_2Cl + 2RMgBr \longrightarrow R-CH_2-C\equiv C-CH_2-R$$

($R = CH_3, C_2H_5, C_3H_7, C_4H_9$)



$$R-\underset{Cl}{CH}-C\equiv C-\underset{Cl}{CH}-R + 2CH_3MgBr \longrightarrow R-\underset{CH_3}{CH}-C\equiv C-\underset{CH_3}{CH}-R$$

($R = CH_3, C_2H_5, C_3H_7$)

Continuing our investigation of the reaction between organomagnesium compounds and unsaturated 1,4-dihalides containing labile halogen atoms, we have extended it to the 1,4-dichloride of cyclopentadiene. In a previous communication [9] we described our preliminary experiments on the reaction of cyclopentadiene dichloride with methyl magnesium bromide. It was established for the first time that the dichloride exchanges each chlorine atom for the radical of the organomagnesium compound to form dimethylcyclopentene (yield 20% of the theoretical).

In the last two years two attempts to realize such a reaction with the aim of synthesizing 3,5-dialkylcyclopentenes have been described in the literature. The dibromide of cyclopentadiene was used in both investigations. Reid and Vost [10] in studying this reaction arrived at the conclusion that cis- and trans-3,5-dibromo-cyclopentenes (1,4-dibromides of cyclopentadiene) do not react in the normal way with organomagnesium compounds but form only polymers. In the literature [11] is described a reaction between cis- and trans-3,5-dibromocyclopentadienes and ethyl magnesium bromide; diethylcyclopentene was isolated from the reaction products in a yield of 25% of the theoretical; in the authors' words this compound consisted "partly at least of 3,5-diethylcyclopentene". The reaction of 1,4-dibromocyclopentadiene with octyl magnesium bromide apparently gave a dioctylcyclopentene in which the position of the octyl groups was likewise not established. Consequently the structure of the hydrocarbons formed in these reactions was not conclusively established by the authors.

In the present research a close study was made of the reaction between organomagnesium compounds and cyclopentadiene dichloride. Reaction of cyclopentadiene 1,4-dichloride with organomagnesium compounds might serve as a method of synthesis of 3,5-dialkylcyclopentenes -1 (II), hydrogenation of which might yield the difficultly accessible 1,3-dialkylcyclopentanes:*

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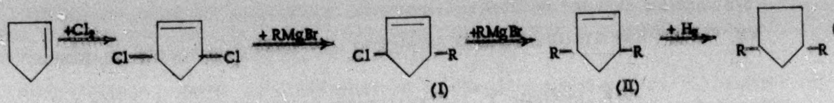
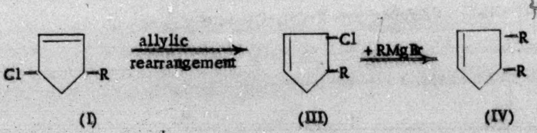
* 3,5-Dialkylcyclopentenes are also interesting because derivatives of one of them —3,5-disec.butylcyclopentene — are auxins a and b (plant-growth promoters [12]).



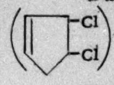
(1)

Since, however, the intermediately formed monochloride (I) is susceptible to allylic rearrangement to the isomeric monochloride (III), the reaction may also lead to formation of a second hydrocarbon —3,4-dialkylcyclopentene-1 (IV):

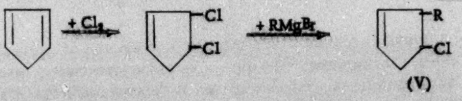


(2)

It must also be noted that the starting cyclopentadiene chloride could also contain the 1,2-dichloride

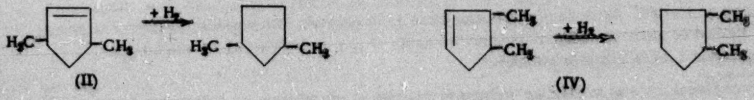


which possesses only one labile chlorine atom. The presence of this dichloride need not interfere with the reaction with the organomagnesium compound because —as we have previously shown [2] —unsaturated 1,2-dichlorides (e.g. butadiene 1,2-dichloride), on reaction with organomagnesium compounds, rearrange to 1,4-dichlorides which also enter into further reaction; in that event, even if the 1,2-dichloride should after all remain in the reaction mixture, then one of the reaction products would be the monochloride (V) which does not belong to the allyl chloride series and does not enter into further substitution reaction; for this reason, it should be an easy matter to separate the resultant hydrocarbons (II and IV):



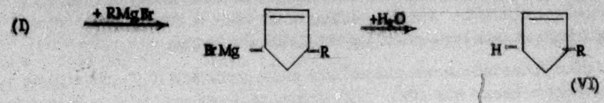
(3)

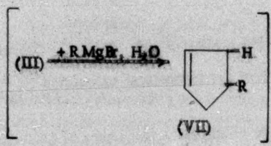
The investigation showed that in the reaction of cyclopentadiene dichloride with methyl magnesium bromide, both possible reaction products —3,5-dimethylcyclopentene-1 (II) and 3,4-dimethylcyclopentene-1 (IV) —are formed in a total yield of 20% of the theoretical; as evidence of this reaction course, hydrogenation of this hydrocarbon mixture gave a catalyzate containing (as demonstrated by the Raman spectrum) 1,3-dimethylcyclopentane (in the cis- and trans- forms) (approx. 60-70%) and 1,2-dimethylcyclopentane (trans-form) (approx. 40-30%):



Thus, during the reaction, allylic rearrangement does actually take place of the initially formed monochloride (I) (see equation 2).

Study of the reaction between cyclopentadiene dichloride and other organomagnesium compounds (ethyl magnesium bromide and propyl magnesium bromide) showed that with them the reaction likewise proceeds in the same direction, i.e., the intermediately formed monochloride (I) is reduced to 3-alkylcyclopentene-1 (VI) [with possible admixture of 4-alkylcyclopentene-1 (VII)]:





This reaction is a secondary one when using ethyl magnesium bromide [yield of ethylcyclopentene (VI) is 5% and that of the diethylcyclopentenes (II) and (IV) is 12% of the theoretical] but is the sole reaction when using propyl magnesium bromide (the yield of propylcyclopentene is 7% of the theoretical); dipropylcyclopentene is not formed at all. Consequently with increasing size of carbon chain in the radical of the organomagnesium compound, this side reaction becomes predominant. Formation of high-boiling polymers is observed in all the reactions that we studied.

On the basis of the experimental data of this investigation of the reaction between cyclopentadiene dichloride and organomagnesium compounds, the above equations (1-5) may be considered to reflect all possible directions of the reaction.

EXPERIMENTAL

Chlorination of cyclopentadiene. Into a solution of 33 g (0.5 mole) cyclopentadiene * in absolute ether (1:1 by volume) was introduced, with salt-snow cooling, dry chlorine until the weight had increased by 35.5 g (0.5 mole). After distilling off the ether (in vacuum in a nitrogen stream) and fractional distillation of the reaction product in vacuum in a stream of nitrogen (in a tall column) there was obtained 41 g dichlorocyclopentene (yield 60% of the theoretical calculated on the cyclopentadiene):

B.p. 35° (5 mm); 50° (10 mm); n_D^{20} 1.5026; d_4^{20} 1.2193; MR_D 33.20. $C_5H_6Cl_2 \ulcorner$. Calculated: MR_D 32.36; EM_D 0.84. Occurrence of an exaltation of the molecular refraction is characteristic of unsaturated 1,4-dichlorides of the allyl type [2,3].

3.885 mg substance: 2.020 mg Cl_2. 5.740 mg substance: 2.970 mg Cl_2. Found %: Cl 51.99, 51.75. $C_5H_6Cl_2$. Calculated %: Cl 51.76.

Dichlorocyclopentene rapidly darkens in the air and turns yellow even when kept in a sealed ampoule under nitrogen.

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* The cyclopentadiene was prepared by depolymerization of the dimer by the method described by B. A. Kazansky and E. M. Terentyev [13]. Technical cyclopentadiene dimer was first washed with concentrated caustic alkali and then with water, dried with calcium chloride and distilled in vacuum (b.p. 70° at 24 mm).

By analogy with the formation of the stereoisomeric 1,4-dibromides on bromination of cyclopentadiene, we may conclude that the dichloride is cyclopentadiene 1,4-dichloride.

In each experiment the dichloride was accompanied by a considerable amount of higher boiling fractions apparently containing cyclopentadiene tetrachlorides. The chlorination of cyclopentadiene has not been described in the literature.

Reaction of cyclopentadiene dichloride with methyl magnesium bromide. To the methyl magnesium bromide prepared from 520 g (5.2 moles) methyl bromide and 96 g magnesium was added, with constant stirring and cooling with snow and salt, an ethereal solution of 120 g (0.88 mole) freshly distilled (in a nitrogen stream) cyclopentadiene dichloride. After the addition of the whole of the dichloride, stirring was continued for another 3 hours at room temperature and for 4 hours with heating.

Decomposition of the reaction mixture was effected with dilute acetic acid (2 N); the aqueous solution was separated and twice extracted with ether. After working up the ethereal solution in the usual manner and distilling off the ether, the residue was distilled off from polymers, boiled in presence of sodium and twice distilled over sodium. The polymer- and halogen compound-free reaction product was distilled over sodium in a column with 50 theoretical plates; a hydrocarbon fraction (dimethylcyclopentenes) was obtained with the following constants:

B.p. 81-82°* (751 mm); n_D^{20} 1.4200; d_4^{20} 0.7614; MR_D 31.96. C_7H_{12} F. Calculated: MR_D 31.86.

The yield of hydrocarbon was 16 g or 20% of the theoretical calculated on the cyclopentadiene dichloride.

The Raman spectrum of the 81-82° fraction contained a frequency of 1613 cm^{-1}. This showed that the fraction contained a cyclopentene hydrocarbon (or a mixture of cyclopentenes) with alkyl groups not located at the double bond; both 3,5-dimethylcyclopentene-1 (II) and 3,4-dimethylcyclopentene-1 (IV) possess such a structure. Hydrocarbons with this structure are characterized by the presence in the Raman spectrum of the 1612-1619 cm^{-1} lines [14]; cyclopentene hydrocarbons whose alkyl groups are linked to non-double-bond carbons are distinguished by the frequency range of approximately 1650-1680 cm^{-1} [14].

3,5- and 3,4-Dimethylcyclopentenes-1 —possible products of the reaction —have not been described in the literature.

The obtained mixture of dimethylcyclopentenes was hydrogenated at 150° over nickel-on-alumina. The catalyzate was distilled over sodium in a column with 25 theoretical plates:

B.p. 89.5-90.5° (756 mm); n_D^{20} 1.4113, d_4^{20} 0.7457; MR_D 32.71. C_7H_{14}. Calculated: MR_D 32.33.

10.380 mg substance: 32.560 mg CO_2; 13.410 mg H_2O. 10.640 mg substance: 33.320 mg CO_2; 13.840 mg H_2O. Found %: C 85.60, 85.46; H 14.46, 14.56. C_7H_{14}. Calculated %: C 85.71; H 14.29.

Literature data for the possible components of the catalyzate: 1,3-dimethylcyclopentane (mixture of isomers) [15] b.p. 89.5-90.6° (760 mm); n_D^{20} 1.4092; d_4^{20} 0.7460; trans-1,2-dimethylcyclopentane [16] b.p. 91.2-91.5° (755 mm); n_D^{20} 1.4126; d_4^{20} 0.7520.

Since it was impossible to fractionate these closely boiling hydrocarbons by distillation in a column, the catalyzate was examined by Raman spectrography.

The spectra of the catalyzate and of the synthetic preparations of 1,3-dimethylcyclopentane (mixture of cis- and trans-isomers) and 1,2-dimethylcyclopentane (trans-isomer) are enumerated in Table 1.

Investigation of the Raman spectrum of the catalyzate and its comparison with the literature data for the spectra of synthetic preparations of 1,3- and 1,2-dimethylcyclopentane showed that the catalyzate contains about 60-70% 1,3-dimethylcyclopentane (in the cis- and trans- forms) and about 40-30% 1,2-dimethylcyclopentane (in the trans-form).** The quantitative composition of the catalyzate was calculated from the intense lines of its spectrum (Table 1): 516, 802 and 828 cm^{-1}, which are characteristic of 1,2-dimethylcyclopentane (mixture of the cis- and trans- forms) and from the 769 and 897 cm^{-1} lines

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* Apart from the 81-82° fraction, there was isolated a 61-67° fraction (2.5 g) which apparently contained methylcyclopentenes (see equations 4 and 5).

** Judging by the Raman spectrum, the catalyzate did not contain cis-1,2-dimethylcyclopentane.

TABLE 1

Raman Spectra		
Of the catalyzate obtained by halogenation	Of 1,3-dimethylcyclopentane (mixture of cis- and trans-isomers)[15]	Of trans-1,2-dimethylcyclopentane [15]
272 (0.7; w)*; 322 (1); 367 (1);	272 (0); 358 (0); 373 (3; w);	278 (0; w); 326 (0);
397 (0.5); 432 (1); 496 (2);	409 (0); 426 (3; w);	364 (0); 497 (35);
516 (3); 550 (0.5); 592 (0.5);	514 (13); 549 (3);	527 (5); 586 (0);
706 (0.5); 769 (2); 802 (3.5);	591 (3; w, W)	607 (4; w); 721 (0);
829 (5); 844 (0); 897 (3);	726 (0); 803 (13; w);	766 (27; W);
956 (2; W); 983 (2);	828 (28); 878 (0);	798 (0); 861 (5);
1025 (1.5; w); 1056 (0);	950 (3); 985 (8);	896 (34); 957 (5; w);
1079-85 (1.5; w); 1099 (3.5);	1021 (3; w); 1041 (3; w);	1005 (4); 1022 (5);
1144 (2.5); 1160 (2);	1085 (3); 1101 (3);	1081 (13; w);
1190 (3); 1258 (0.5);	1140 (11); 1152 (11);	1147 (10); 1186 (3; w);
1292 (1.5); 1315 (1.5);	1188 (2; w); 1251 (0);	1205 (3; w); 1283 (2);
1345 (2); 1374 (1);	1298 (2; w); 1314 (8);	1303 (2); 1340 (5);
1460 (10; w).	1346 (5); W); 1457 (40; w).	1360 (3); 1457 (40; w, W).

which are characteristic of 1,2-dimethylcyclopentane (trans-form). On the basis of these data it is obvious that the product of reaction between cyclopentadiene dichloride and methyl magnesium bromide comprises two hydrocarbons (see equations 1 and 2); the normal product of reaction is 3,5-dimethylcyclopentene-1 (about 60-70 %) together with 3,4-dimethylcyclopentene-1 (about 40-30%) due to allylic rearrangement of the monochloride (I); hydrogenation of these hydrocarbons also gave a mixture of 1,3- and 1,2-dimethylcyclopentanes.

Reaction of cyclopentadiene dichloride with ethyl magnesium bromide. The reaction between cyclopentadiene dichloride (1.2 moles) and ethyl magnesium bromide and separation of the reaction products were carried out by the above-described method. Distillation of the hydrocarbon fraction (freed from halogen compounds and from polymers) over sodium in a column with 50 theoretical plates gave two fractions: I with b.p. 97° (763 mm) and II with b.p. 140.3° (763 mm). Judging by its constants and analytical data, the second fraction was a mixture of diethydcyclopentenes — 3,5-diethylcyclopentene-1 and 3,4-diethylcyclopentene-1 (by analogy with the products of reaction of cyclopentadiene dichloride with methyl magnesium bromide).

B.p. 140.3° (763 mm; n_D^{20} 1.4390; d_4^{20} 0.7922; MR_D 41.24. C_9H_{16} ⌈. Calculated: MR_D 41.09.

4.160 mg substance: 13.270 mg CO_2; 4.870 mg H_2O. 4.460 mg substance: 13.900 mg CO_2; 5.070 mg H_2O. Found %: C 87.05, 87.03; H 13.10, 12.72. C_9H_{16}. Calculated %: C 87.04; H 12.96.

The yield was 18 g or 12% of the theoretical calculated on cyclopentadiene dichloride.

Literature data: Of the two possible products of reaction, 3,4-diethylcyclopentene-1 (IV) has not been described in the literature, and 3,5-diethylcyclopentene-1 has only been mentioned in a recent paper [11]; the authors give the name of 3,5-diethylcyclopentene to the hydrocarbon that they obtained by reacting ethyl magnesium bromide with the 1,4-dibromide of cyclopentadiene, and they report the following constants:

B.p. 141°; n_D^{20} 1.4390; d_4^{20} 0.7921.

There is no doubt that the hydrocarbon of the American authors was not a pure 3,5-diethylcyclopentene but a mixture of isomers, similar to the one that we obtained in the experiment with cyclopentadiene dichloride.

The lower boiling fraction (b.p. 97°), judging by its constants and the analytical data, was 3-ethylcyclopentene-1 (VI) [possibly contaminated with 4-ethylcyclopentene-1 (VII)], formed by a side reaction

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* Intensities were measured visually in the ten-ball scale.

(see equation 4): b.p. 97° (763 mm); n_D^{20} 1.4310; d_4^{20} 0.7828; MR_D 31.82. C_7H_{12}F. Calculated: MR_D 31.85.

6.750 mg substance: 21.620mg CO_2; 7.660 mg H_2O. 4.862 mg substance: 15.570 mg CO_2; 5.465 mg H_2O. Found %: C 87.41, 87.39; H 12.70, 12.58. C_7H_{12}. Calculated %: C 87.44; H 12.58.

The yield was 5% of the theoretical, calculated on cyclopentadiene dichloride.

Literature data for 3-ethylcyclopentene-1 [17]: b.p. 96.7-98.8° (760 mm); n_D^{20} 1.4319; d_4^{20} 0.7835.

Optical investigation confirmed that the isolated hydrocarbon was 3-ethylcyclopentene (VI), at least in the main. The Raman spectrum of the prepared ethylcyclopentene contained all the lines found in the spectrum of the synthetic preparation of 3-ethylcyclopentene-1 (prepared by reaction of 3-chlorocyclopentene with ethyl magnesium bromide [17] (Table 2).

Reaction of cyclopentadiene dichloride with propyl magnesium bromide. This reaction led to formation of only 3-propylcyclopentene-1 (VI) (possibly contaminated with 4-propylcyclopentene-1), which had the following constants after distillation over sodium in a column with 25 theoretical plates:

B.p. 125° (758 mm); n_D^{20} 1.4370; d_4^{20} 0.7918; MR_D 36.47. C_8H_{14}F Calculated: MR_D 36.48.

3.570 mg substance: 11.415 mg CO_2; 4.020 mg H_2O. 4.690 mg substance: 14.395 mg CO_2; 5.335 mg H_2O. Found %: C 87.26, 87.25; H 12.60, 12.73. C_8H_{14}. Calculated %: C 87.20; H 12.80.

The yield was 7% of the theoretical, calculated on the cyclopentadiene dichloride.

Literature data [18]: b.p. 125.9°; n_D^{20} 1.4359; d_4^{20} 0.7910.

TABLE 2

Raman spectra	
Of ethylcyclopentene prepared in the present investigation	Of synthetic preparation of 3-ethylcyclopentene [17]
295 (1);* 322 (1.2; w); 392 (3);	306 (5; w ; d); 322 (6; w ; d);
470 (2); 489 (1.5); 587 (1; w);	397 (11.5); 473 (9); 493 (7);
719 (1); 746 (0.3; h); 785 (1.5);	590 (5; d); 722 (3; d); 757 (2; d);
852 (2.5); 880 (0.8); 909 (8);	787 (3; d); 855 (11); 913 (20);
935 (5); 958 (1); 994 (0.8);	938 (10); 963 (3); 996 (6.5);
1054 (2; w); (1081 (0.5); 1092 (11);	1056 (11); 1096 (23); 1120 (17; w; h);
1101 (1.5); 1117 (1.5); 1170 (2);	1173 (45); 1204 (2.5; d);
1198 (2; w); 1241 (0.5); 1263 (0.3);	1263 (3;d); 1285 (5); 1317 (6);
1278 (4; w); 1310 (1.5); 1340 (1);	1343 (4); 1361 (12); 1385 (7);
1357 (2); 1357 (2); 1382 (0.5);	1443 (22.5; w); 1462 (17); 1617 (35).
1439 (10; w); 1459 (4); 1591 (0.3); 1613 (16)	

* Intensities were determined visually; the intensity of the 1439 cm^{-1} line was assumed to be equal to ten arbitrary units.

The Raman spectrum contained the 1612 cm^{-1} line, characteristic of the non-alkylated double bond in the cyclopentene series of hydrocarbons [14]. Dipropylcyclopentene was not detected among the reaction products; consequently the reaction proceeded in one direction only (according to equation 4) with formation of propylcyclopentene.

SUMMARY

1. A study was made of the reaction between cyclopentadiene dichloride and organomagnesium compounds (methyl, ethyl and propyl magnesium bromides).

2. It was established that reaction of cyclopentadiene 1,4-dichloride with methyl magnesium bromide resulted in both atoms of halogen being successively replaced by methyl groups with formation of the normal product of reaction — 3,5-dimethylcyclopentene-1; but since the intermediately formed 5-chloro-3-methylcyclopentene (I) partially undergoes allylic rearrangement to 3-chloro-4-methylcyclopentene (III) and the latter also enters into reaction with methyl magnesium bromide, a second hydrocarbon is formed in the shape of 3,4-dimethylcyclopentene-1. The mixture of hydrocarbons is formed in a total of 20% of the theoretical and contains approximately 60-70% of 3,5-dimethylcyclopentene-1 and 40-30% of 3,4-dimethylcyclopentene-1.

3. Reaction of cyclopentadiene 1,4-dichloride with ethyl magnesium bromide gives, apart from a mixture of diethylcyclopentenes (yield 12% of the theoretical), 3-ethylcyclopentene-1 (yield 5% of the theoretical). This hydrocarbon is the product of secondary reduction of an intermediately formed monochloride (I) (5-chloro-3-ethylcyclopentene).

4. Reaction of cyclopentadiene 1,4-dichloride with propyl magnesium bromide did not give dipropylcyclopentenes among the reaction products; the only hydrocarbon to be isolated was 3-propylcyclopentene-1 (7% of the theoretical), formed by the above-mentioned secondary reaction.

Considerable amounts of polymers were observed to be formed in all the reactions investigated.

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THE DECOMPOSITION OF TRIMETHYLCROTYLAMMONIUM HYDROXIDE

Ya. M. Slobodin and I. N. Shokhor

Of the methods of obtaining unsaturated hydrocarbons, great interest attaches to the one involving decomposition of completely substituted ammonium bases. There are several statements in the literature (by Chugaev, Demyanov and others) to the effect that decomposition of the bases proceeds without isomerization, so that this method ought to yield "normal" products of reaction. It is clear that this generalization is not without exceptions. For example, in the exhaustive methylation of piperidine the last stage gives a quantitative yield of piperylene instead of the "normal" reaction product — a hydrocarbon with isolated bonds [1].

We have established that decomposition of a pyrrolidine base gives an "anomalous" product with conjugated bonds in place of the anticipated product with isolated or allenic bonds. [2].

The foregoing facts show that decomposition of completely substituted ammonium bases containing an unsaturated radical as one of the substituents leads to formation of compounds with conjugated bonds instead of "normal" compounds with isolated or allenic bonds.

In this investigation we have studied the decomposition of trimethylcrotylammonium hydroxide $CH_3CH{=}CHCH_2N(CH_3)_3OH$.

In the event of a "normal" course of the decomposition, the final product would by methylallene, whereas an "anomalous" course could lead to either butadiene or dimethylacetylene.

Our experiments showed that the only hydrocarbon formed in the decomposition of trimethylcrotylammonium hyroxide is butadiene.

The starting material for the preparation of trimethylcrotylammonium hydroxide was crotyl alcohol, treatment of which with PCl_3 gave crotyl chloride.

In the Raman spectrum of crotyl chloride the double bond was represented by the 1673 cm^{-1} line. The absence from the spectrum of a line in the 1640 cm^{-1} region shows that our crotyl chloride was substantially free from its allyl isomer — 3-chlorobutene-1.

Reaction of crotyl chloride with excess of trimethylamine gave trimethylcrotylammonium chloride. Distillation of the latter with a small excess of 40% aqueous KOH decomposed it with formation of butadiene.

EXPERIMENTAL

Crotyl chloride. 40 g crotyl alcohol, prepared by reduction of crotonaldehyde with aluminum isopropylate [3], was mixed with 6 g pyridine and run from a dropping funnel into a flask containing 30 g PCl_3. The contents of the flask were thoroughly stirred while cooling with ice water. After all of the alcohol had been added, stirring was continued for another hour at room temperature. The contents of the flask were then poured into cold water. The chloride was extracted with ether. The ether solution was dried with calcium chloride and the ether distilled off to leave 26 g chloride with b.p. 83-84°; n_D^{20} 1.4352.

Raman spectrum: 352 (8), 488 (2), 672 (6), 782 (5), 1077 (3), 1181 (4), 1243 (5), 1314 (4), 1384 (2), 1449 (5), 1673 (10).

Trimethylcrotylammonium chloride. 26 g crotyl chloride was treated, while being cooled, with double the theoretical amount of trimethylamine. The mixture was held at room temperature for 40 hours. The precipitated trimethylcrotylammonium chloride was filtered off, washed several times with absolute ether and dried in vacuum.

0.1448 g substance: 9.70 ml 0.1 N $AgNO_3$. Found %: Cl 23.77. Calculated %: Cl 23.74.

Preparation of the hydrocarbon. Into a flask were charged 15 g trimethylcrotylammonium chloride and a small excess over the theoretical of 40% KOH solution free from carbonate. The distillation flask was connected to a condenser and the receiver was cooled with ice water. The volatile products not condensing at 0° were trapped in a test tube cooled with dry ice. The ammonium base started to decompose during distillation. Heating was continued until the formation of decomposition products had substantially ceased. The contents of the receiver were acidified with sulfuric acid solution. No insoluble compounds were detected. In the test tube (cooled with dry ice) was a readily mobile liquid which distilled without residue below 0°. Its vapor was passed through a sulfuric acid washer for removal of any trimethylamine, after which it was transferred to a flask containing bromine. A crystalline bromide with m.p. 114° was formed. After crystallization from alcohol the m.p. was 117°. A mixed melting test with butadiene tetrabromide did not give a depression.

SUMMARY

Decomposition of trimethylcrotylammonium hydroxide gives butadiene. Formation of appreciable amounts of the "normal" product —methylallene—was not observed.

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THE ORDER OF ADDITION OF ALCOHOLS TO TRIMETHYLETHYLENE OXIDE

A. A. Petrov, B. V. Gantseva, and O. A. Kiseleva

In previous investigations one of the present authors established the general rule that the order of addition to asymmetrical organic α-oxides of different substances is determined by their acid-base character or by the nature of the catalyst used [1]. In an alkaline medium the addition proceeds exclusively (or almost so) according to the Markovnikov rule [2], whereas in an acid medium isomeric compounds are obtained to a greater or lesser extent. Thus, in the presence of alcoholates, the primary-secondary propylene oxide reacts with alcohols to give primary ethers of propylene glycol, but in presence of acids or boron fluoride a mixture of primary and secondary ethers is formed. The primary-tertiary 1,2-epoxy-2-methylpropane in presence of alcoholates forms primary ethers of isobutylene glycol, and in presence of acids or boron fluoride it gives tertiary ethers of isobutylene glycol. Such an order of addition of alcohols to propylene oxide is confirmed by a series of investigations by foreign authors [3,4]. In precisely the same way there is a sharp difference in the order of addition of alcohols to butadiene oxide depending upon the character of the catalyst [5, 6, 7]; this is also true of other unsaturated oxides, for example styrene oxide [8], 2-methyl-1-butene-3-yne oxide [9], etc. This law, discovered for the reaction of asymmetrical oxides with alcohols, evidently has a general character and may be extended to the reactions of these oxides with other components, in particular to hydrogenation reactions [10, 11].

As a further contribution to knowledge in this field, it was of undoubted interest to study the order of addition of alcohols to the secondary-tertiary trimethylethylene oxide and to compare it with the order of addition of the same compounds to primary-secondary and primary-tertiary α-oxides.

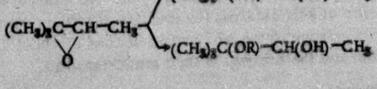
Trimethylethylene oxide is a representative of a class of little investigated substances. It was first prepared by Eltekov [12] by the action of caustic alkali on trimethylethylene chlorohydrin. Studies have been made of the addition to it of water [12], hydrogen halides [13], organometallic compounds [14-16], and ammonia and amines [17-20]. Ammonia and amines (dimethylamine, diethylamine, piperidine and benzylamine), as bases, add on strictly according to the Markovnikov rule. With hydrogen chloride, the reaction proceeds contrary to the Markovnikov rule and the main product is the secondary alcohol.

Of considerable interest is the reaction of trimethylethylene oxide with simple and mixed organometallic compounds. In both cases the reaction proceeds with rupture of the oxide bond at the secondary carbon atom with formation of tertiary alcohols. In this instance, therefore, organomagnesium compounds react like alkaline components.

A. A. Tyazhelova [21] has studied the reaction of trimethylethylene oxide with alcohols in presence of alcoholates. She obtained monoethers of trimethylethylene glycol from ethyl through isoamyl, but their structure was not established. Nor was the effect of the nature of the catalyst examined.

Our experiments have shown that trimethylethylene oxide and alcohols give entirely different substances in acid and alkaline media.

Reaction of trimethylethylene oxide with alcohols would be expected to yield secondary or tertiary ethers of trimethylethylene glycol according to the scheme:



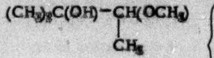
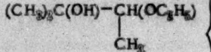
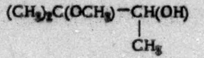
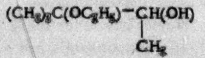
$$(CH_3)_2C(OH)-CH(OR)-CH_3$$
$$(CH_3)_2C(OR)-CH(OH)-CH_3$$

Addition of methyl and ethyl alcohols in presence of sodium alcoholate gave exclusively secondary ethers of 2-methylbutanediol [2,3]. The ethyl ether of this glycol, as already noted, was prepared by A. A. Tyazhelova. It is also reported that it can be prepared by the action of methyl magnesium iodide on the ethyl ester of α-ethoxypropionic acid [22], as well as by other methods [23].

With the aim of elucidating the structure of the products of reaction of trimethylethylene oxide with methyl and ethyl alcohols in an alkaline medium, we prepared the anticipated secondary ethers of trimethylethylene glycol by the action of methyl magnesium iodide on the methyl ester of α-methoxypropionic acid and on the ethyl ester of α-ethoxypropionic acid.

The constants of the ethers prepared from trimethylethylene oxide and from the full esters of lactic acid, as set out in Table 1, are seen to be substantially identical. Since the structure of the esters prepared by the latter method is not subject to doubts, it is established that the substances prepared from the oxide are secondary monoethers of trimethylethylene glycol.

TABLE 1

Substance	B. p. °C	d_4^{20}	n_D^{20}	MR_D		Method of preparation
				Found	Calcd.	
 $(CH_3)_2C(OH)-\underset{\displaystyle CH_3}{\underset{\vert}{C}}H(OCH_3)$	131-132.5	0.8963	1.4130	32.88	33.08	From trimethylethylene oxide in presence of alcoholate.
	131-132.5	0.8934	1.4128	32.97	33.08	From methyl ester of methoxypropionic acid.
 $(CH_3)_2C(OH)-\underset{\displaystyle CH_3}{\underset{\vert}{C}}H(OC_2H_5)$	142-143	0.8756	1.4120	37.59	37.69	From trimethylethylene oxide in presence of alcoholate.
	142-147	0.8754	1.4136	37.68	37.69	Details by A. A. Tyazhelova [21].
	142-143	0.8732	1.4118	37.65	37.69	From ethyl ester of ethoxypropionic acid.
	140-141	–	1.4111	–	–	Details by Stevens for the L-form [23].
 $(CH_3)_2C(OCH_3)-\underset{\displaystyle CH_3}{\underset{\vert}{C}}H(OH)$	143-144	0.9177	1.4220	32.72	33.08	From trimethylethylene oxide in presence of boron fluoride.
 $(CH_3)_2C(OC_2H_5)-\underset{\displaystyle CH_3}{\underset{\vert}{C}}H(OH)$	152.5-154	0.8982	1.4208	37.31	37.69	

The tertiary character of the hydroxyl in these substances was confirmed by investigation of their behavior toward acetic anhydride. Acetic anhydride in presence of a drop of sulfuric acid gives the acetates in 50% yield. In the conditions of this reaction, considerable dehydration of the glycol ether takes place with formation of methylisopropyl ketone.

The constants of the acetates are given in Table 2.

TABLE 2

Compound	B.p. °C	d_4^{20}	n_D^{20}	MR_D	
				Found	Calcd.
$(CH_3)_2C(OCOCH_3)-CH(OCH_3)-CH_3$	158-161	0.9460	1.4118	42.12	42.14
$(CH_3)_2C(OCOCH_3)-CH(OC_2H_5)-CH_3$	169-170	0.9243	1.4108	46.78	47.06
$(CH_3)_2C(OCH_3)-CH(OCOCH_3)-CH_3$	168-170	0.9523	1.4140	42.04	42.44

In presence of sulfuric acid or boron fluoride, methyl and ethyl alcohols add on to trimethylethylene oxide with formation of monoethers of trimethylethylene glycol, markedly different in constants from the already characterized secondary monoethers. Since addition of alcohols to trimethylethylene oxide can only yield two forms of monoethers, we are bound to attribute to the substances formed in presence of acid catalysts the structure of tertiary ethers. This structure was confirmed by their oxidation with chromic acid mixture to the previously described ethers of dimethylacetyl carbinol which were identified by their melting point and the analyses of their semicarbazones.

Due to the fact that these ethers contain a secondary hydroxyl group, they are more easily acetylated by acetic anhydride than are their isomers with a tertiary alcohol group. The acetate of this monoether also differs from the isomer in possessing a pleasanter odor. The constants of the acetates are given in Table 2.

Consequently, this investigation has established that the secondary-tertiary trimethylethylene oxide resembles the primary-tertiary 1,2-epoxy-2-methylpropane in its behavior toward alcohols in presence of basic and acid catalysts; it forms differing products in alkaline and acidic media.

EXPERIMENTAL

The starting material for this investigation was dimethylethyl carbinol prepared by Grignard synthesis from ethyl bromide and acetone.

Dimethylethyl carbinol was converted into the amylene by slow distillation in a dephlegmator on a water bath over an equal amount of crystalline oxalic acid (the alcohol was added dropwise to the heated acid with continuous distillation). From 150 g carbinol was obtained 86 g trimethylethylene with b.p. 37.5-38.5°. Yield 72%.

Trimethylethylene was converted into the chlorohydrin by the action of a solution of monochlorourea by the method previously described by one of us [13]. From 86 g trimethylethylene was obtained 84 g chlorohydrin (yield 56%) and 5 g water-insoluble products.

The chlorohydrin was converted into the oxide by slow distillation over concentrated KOH solution on the water bath (the chlorohydrin was run dropwise into the heated alkali). From 84 g chlorohydrin was obtained 46.5 g oxide. Yield 79%.

The trimethylethylene oxide with which we worked had the constants: b.p. 73-76°; d_4^{20} 0.8065, n_D^{20} 1.3860. Previously found constants were: b.p. 73-74°; d_4^{20} 0.8098, n_D^{20} 1.3860.

Trimethylethylene oxide was reacted with alcohols in the following conditions.

In 2 moles of the alcohol was dissolved 0.75 g metallic sodium, and to the solution was added 8.6 g (0.1 mole) oxide. The mixture was heated in sealed glass tubes at 100° for 20 hours, after which the tubes were opened and the reaction mixture fractionated in an efficient dephlegmator. The yield of ethers was 45-50%. In one experiment with methyl alcohol when heating was for a total of 6 hours at the boiling point of the alcohol, the yield of ether was negligibly small.

Analytical data for the prepared ethers are set forth in Table 4.

The starting material for the preparation of secondary ethers of trimethylethylene glycol by another method was ethyl bromoacetate.

90 g ester was gradually added through a reflux condenser to a solution of Na alcoholate prepared from 30 g sodium and 200-250 ml methyl or ethyl alcohol. After boiling for 2-3 hours, addition was made to the mixture of water, after which it was distilled until the whole of the alcohol had been removed. The mixture was then acidified with 25% sulfuric acid and the alkoxypropionic acid was extracted with ether. The yield of methoxypropionic acid was 68%, that of ethoxypropionic acid 71%.

The constants of the prepared compounds are presented in Table 3 with the literature data.

TABLE 3

Substance	B.p. °C	Pressure (in mm)	d_4^{20}	n_D^{20}	MR_D Found	MR_D Calcd.
$CH_3-CH(OCH_3)-COOH$	87-88	10	1.0915	1.4148	23.87	23.85
ditto [26]	87-89	10	–	–	–	–
$CH_3-CH(OC_2H_5)-COOH$	95	10	1.0375	1.4155	28.54	28.47
ditto [24]	97	11	–	–	–	–
$CH_3-CH(OCH_3)-COOCH_3$	130-131	760	0.9969	1.3968	28.52	28.47
ditto [24]	129.5	752	1.0024	1.3968	28.37	28.47
$CH_3-CH(OC_2H_5)-COOC_2H_5$	153-153.5	760.	0.9402	1.4012	37.79	37.71
ditto [24]	155	760	0.9446	1.4012	37.62	37.71

The alkoxypropionic acids were converted into the corresponding esters by saturation of their alcoholic solutions with hydrogen chloride. After standing for 24-48 hours, these solutions were neutralized with sodium carbonate and the reaction products were extracted with ether.

The yield of methyl α-methoxypropionate was 68%, that of the ethyl α-ethoxypropionate was 77.5%. The constants of the esters are presented in Table 3.

Methyl magnesium iodide was reacted with both of the esters in the following conditions. To a solution of CH_3MgI, prepared from 9 g Mg, was added (with mechanical stirring and ice cooling) an ethereal solution of the ester of the alkoxypropionic acid. After standing for a few hours, the reaction mixture was carefully poured into a mixture of ice and a saturated ammonium chloride solution. The ethereal solution was separated. The aqueous solution was again extracted with ether. The ethereal solutions were washed with saturated ammonium chloride solution and then with water and dried over calcined sodium sulfate.

Yield of methyl ester 72%, of ethyl ester 78%. Constants are given in Table 1.

Acetylation of the esters was studied in the following conditions. To a mixture of 4.2 g methyl ester and 5.5 g acetic anhydride (50% excess) was added with cooling a drop of sulfuric acid. Heat was developed after a short period. The reaction mixture was washed with water and with saturated sodium carbonate solution and then distilled. The following fractions were obtained: 1) 90-100°; 2) 109-150°; 3) 155-161°; 4) residue.

With p-nitrophenylhydrazine in acetic acid solution, the first fraction gave the characteristic p-nitrophenylhydrazone of methylisopropyl ketone with m.p. 103-104° (from alcohol).

The third fraction was redistilled. The greater part came over at 158-161° and consisted of the acetate of the alcohol concerned. Yield 50%. The constants appear in Table 2 and the analytical data in Table 4.

Addition of alcohols to trimethylethylene oxide was studied in the following conditions in presence of sulfuric acid. To a solution of 6 g oxide in 75 ml methyl alcohol was added 0.5 ml concentrated sulfuric acid. The temperature rose quickly to 45-50°. After standing for several hours, the sulfuric acid was neutralized with caustic alkali and the mixture distilled through a dephlegmator. In this way about 3 g ether (yield 25%) with the constants listed in Table 1, was obtained.

Treatment of a solution of 8 g oxide in 75 ml methyl alcohol with 0.5 ml boron fluoride etherate caused considerable heat to be developed. The subsequent usual treatment of the mixture gave about 5 g ether. Yield 42%.

In the same conditions the ethyl ether was also obtained in a yield of 42%. A by-product was methylisopropyl ketone.

Oxidation of the tertiary methyl ether of trimethylethylene glycol was performed in the following conditions. To a solution of 2 g of the ether and 0.9 g of sodium bichromate in 25 ml acetic acid (80%) with stirring and cooling (20-25°) was added dropwise a double excess of 25% sulfuric acid. After neutralization of the mixture, the oxidation products were extracted with ether. In this way about 1 g of substance distilling at 122-132° and with n_D^{20} 1.4100, was obtained. The constants reported in the literature for dimethylacetyl carbinol [25] are b.p. 124-127° and n_D^{20} 1.4100.

From the products of oxidation was obtained a semicarbazone with m.p. 162°, which agrees with the literature data for the methyl ether of dimethylacetylcarbinol semicarbazone.

4.65 mg substance: 9.3 ml N_2 (13°, 759 mm). Found %: N 23.84. $C_7H_{15}O_2N_3$. Calculated %: N 24.26.

From the products of oxidation in the same conditions of the ethyl ether of trimethylethylene glycol was obtained a semicarbazone with m.p. 172°, which agrees with the literature data for the semicarbazone of the ethyl ether of the dimethylacetyl carbinol.

TABLE 4

Substance	Wt. of sample (mg)	CO_2 (mg)	H_2O (mg)	Found %		Calcuated %	
				C	H	C	H
$(CH_3)_2C(OH)-CH(OCH_3)-CH_3$	12.14	27.22	13.18	61.19	12.15	60.98	11.94
$(CH_3)_2C(OH)-CH(OC_2H_5)-CH_3$	10.22	23.78	11.26	63.50	12.33	63.60	12.20
$(CH_3)_2C(OCH_3)-CH(OH)-CH_3$	9.22	20.36	9.73	61.15	11.81	60.98	11.94
$(CH_3)_2C(OC_2H_5)-CH(OH)-CH_3$	17.48	40.78	19.39	63.66	12.42	63.60	12.20
$(CH_3)_2C(OCOCH_3)-CH(OCH_3)-CH_3$	9.12	19.96	8.32	59.72	10.21	59.97	10.07
$(CH_3)_2C(OCOCH_3)-CH(OC_2H_5)-CH_3$	19.15	43.25	18.00	61.64	10.52	62.04	10.41
$(CH_3)_2C(OCH_3)-CH(OCOCH_3)-CH_3$	11.22	25.13	10.41	59.73	10.15	59.97	10.07

Acetylation of the tertiary methyl ether of trimethylethylene glycol was performed in the same conditions as for the isomeric ethers. The yield of acetate was 75%. Constants appear in Table 2 and analytical data in Table 4.

SUMMARY

1. The addition of alcohols to trimethylethylene oxide was investigated in presence of alcoholates, sulfuric acid and boron fluoride.

2. It was established that in presence of alcoholates the addition of alcohols follows the Markovnikov rule and the secondary monoethers of trimethylethylene glycol are formed. The latter were prepared by another method – by the action of methyl magnesium iodide on esters of α-alkoxypropionic acids.

3. In presence of sulfuric acid and boron fluoride the addition of alcohols proceeds with formation of tertiary ethers of trimethylethylene glycol. The structure of the latter was confirmed by oxidation to ethers of dimethylacetyl carbinol which have been described in the literature.

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ALKANE SULFONIC ACIDS

VIII. SYNTHESIS AND PROPERTIES OF ACYLAMIDES OF 2-METHYLETHANE- AND BUTANESULFONIC ACIDS

A. G. Kostsova

We have described acet-, propion- and benzamides of chloromethane-, α-chloromethane-, methane- and ethanesulfonic acids [1]. As already noted, of these derivatives, the benzamides possess an extremely sweet taste (specifically, only the benzamides of alkane- and, in particular, α-chloroalkanesulfonic acids). The benzamides of benzylbenzenesulfonic acids do not possess this property. We thus drew attention to the role of the alkyl and chloroalkyl radicals in imparting a sweet taste to these compounds. This property is induced not only by the alkyl radical but also by its combination with the $SO_2NHCOC_6H_5$ grouping, since acetamides and propionamides with the same alkyl radicals are not sweet.

In the present investigation we prepared and characterized the acet-, propion- and benzamides of 2-methylethane- and butanesulfonic acids. Apart from their preparation, we were interested in the effect of increasing chain length on the sweetness of benzamides. It was found that the benzamide of 2-methylethanesulfonic acid possesses a markedly sweet taste, although weaker than that of the derivatives of chloromethane-, α-chloroethane-, methane- and ethanesulfonic acids. The benzamide of butanesulfonic acid is perfectly tasteless.

The observations made in this investigation permit the conclusion that the sweetness is weakened with increasing chain length and finally disappears. It seems probable that a special function is exercised in respect to this property by methyl and chloromethyl groups directly linked to the benzoylsulfamino grouping. With increasing distance of these radicals from the benzoylsulfamino grouping, the sweetness disappears. The taste of these compounds was only determined organoleptically. The compounds which we prepared are crystalline bodies; the acetamides and propionamides have good solubility in water in the cold, but the benzamides are only soluble when hot. In aqueous solutions they are all weakly acidic (pH 4-5); they readily dissolve in caustic alkalies. The general equation for the reaction is: $RSO_2NH_2 + R'COCl \rightarrow RSO_2NHCOR' + HCl$.

EXPERIMENTAL *

1. Preparation of 2-methylethanesulfonamide. 6.2 g 2-methylethane sulfochloride was dissolved in 50 ml absolute benzene. Into the solution in the course of half an hour was passed a slow stream of dry ammonia at 0°, after which the temperature was raised to 50° and the ammonia was passed in for another half hour. At the end of the reaction, the precipitate of ammonium chloride was filtered off. The benzene was distilled off from the benzene filtrate on the water bath and the oily residue was distilled in vacuum. The unreacted sulfochloride came over, leaving in the flask the amide, which solidified on cooling to a greyish-yellow mass. The amide was extracted from the distillation flask and recrystallized from benzene. The filtered ammonium chloride was repeatedly extracted with benzene (using the benzene distilled off from the reaction mixture). On cooling, the extract deposited white crystals of 2-methylethanesulfamide. Total yield of amide 1.5 g or 35% of theory. M. p. 60°.

2. Preparation of butanesulfonamide. 5 g butanesulfochloride was dissolved in 50 ml kerosene. Into the solution was passed a stream of dry ammonia at −5° for 15 minutes. At the conclusion of the reaction, the kerosene was separated and the amide was isolated from the residue (mixture of amide and ammonium chloride) by repeated extraction. Yield 2.25 g or 51% of the theoretical. Slightly yellow crystals, greasy to the touch; m.p. 43-45°.

3. Preparation of the acetamide of 2-methylethanesulfonic acid. ** 0.5 g 2 methyl ethanesulfonamide

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* V. I. Dubinina and V. A. Malakhov took part in the experimental work.

** Acet- and propionamides were prepared by the same method.

and 0.48 g acetyl chloride were taken. The mixture was refluxed on a boiling water bath for 1½ hours. At the end of the reaction the cooled mixture solidified to a dense grey mass. The product was recrystallized from benzene. M.p. 89°. Yield 0.5 g or 71% of the theoretical. Similar results are obtained by carrying out the reaction with acetic anhydride. 2-Methylethanesulfoacetamide is hygroscopic and has a sour taste.

0.1118 g substance: 6.67 ml 0.1 N H_2SO_4. 0.1506 g substance: 0.2114 g $BaSO_4$. Found %: N 8.35; S 19.24. $C_5H_{11}O_3NS$. Calculated %: N 8.48; S 19.39.

4. Preparation of the acetamide of butanesulfonic acid. 1 g butanesulfonamide and 0.9 g acetyl chloride were taken. Yield of butanesulfoacetamide 1 g or 70% of the theoretical. White platelets, m.p. 68°, sour-astringent taste, hygroscopic.

0.1168 g substance: 6.57 ml 0.1 N H_2SO_4. 0.1032 g substance: 0.1325 g $BaSO_4$. Found %: N 7.87; S 17.66. $C_6H_{13}O_3NS$. Calculated %: N 7.82; S 17.87.

5. Preparation of propionamide of 2-methylethanesulfonic acid. 0.5 g 2-methylethanesulfonamide and 0.45 g propionyl chloride were taken. The crude 2-methylethanesulfopropionamide was recrystallized from a mixture of benzene and gasoline. M.p. 103°. Yield 0.24 g or 35% of the theoretical. Hygroscopic, sour taste.

0.1210 g substance: 6.32 ml 0.1 N H_2SO_4. 0.1012 g substance: 0.1318 g $BaSO_4$. Found %: N 7.31; S 17.32. $C_6H_{13}O_3NS$. Calculated %: N 7.85; S 17.87.

6. Preparation of propionamide of butanesulfonic acid. 1 g butanesulfonamide and 0.8 g propionyl chloride were taken. Yield of butanesulfopropionamide (recrystallized from gasoline-benzene) was 1.1 g or 81% of the theoretical. Colorless plates, m.p. 67°. Sour-astringent taste, hygroscopic.

0.1230 g substance: 6.39 ml 0.1 N H_2SO_4. 0.1640 g substance: 0.1952 g $BaSO_4$. Found %: N 7.27; S 16.31. $C_7H_{15}O_3NS$. Calculated %: N 7.20; S 16.58.

7. Preparation of benzamide of 2-methylethanesulfonic acid. 0.5 g of 2-methylethanesulfonamide and 0.75 g benzoyl chloride were heated on an oil bath at 150-160° under a reflux condenser for 2 hours. The resultant black, viscous oil was transferred to a watch glass for evaporation of the excess of benzoyl chloride. On rubbing with a glass rod while cooling, the viscous oil solidified. The dark-grey 2-methylethanesulfobenzamide was recrystallized from alcohol and water. M.p. 119°. Yield 0.4 g or 55% of the theoretical. Colorless crystals with a slightly sweet taste.

0.1620 g substance: 6.88 ml 0.1 N H_2SO_4. 0.1394 g substance: 0.1444 g $BaSO_4$. Found %: N 5.94; S 14.20. $C_{10}H_{13}O_3NS$. Calculated %: N 6.16; S 14.09.

8. Preparation of benzamide of butanesulfonic acid. 1 g butanesulfonamide and 1.2 g benzoyl chloride were taken. Further procedure as in the preceding experiment. Yield of butanesulfobenzamide 0.6 g or 33.3% of the theoretical. Colorless crystals melting at 65°. Tasteless.

0.1415 g substance: 5.91 ml 0.1 N H_2SO_4. 0.1097 g substance: 0.1033 g $BaSO_4$. Found %: N 5.84; S 12.91. $C_{11}H_{15}O_3NS$. Calculated %: N 5.80; S 13.27.

SUMMARY

1. Acet-, propion- and benzamides of 2-methylethane- and butanesulfonic acids were prepared and characterized.

2. It was noted that the acet- and propionamides possess a sour or sour-astringent taste, 2-methylethanesulfobenzamide has a sweet taste, and butanesulfobenzamide is tasteless.

3. It is shown that the sweet taste of the benzamides of alkanesulfonic acids is weakened with increasing length of aliphatic radical chain and finally disappears.

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THE REACTION OF SULFURYL CHLORIDE WITH VINYL CHLORIDE

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It is known that the reaction of carboxylic acid chlorides with acetylene or vinyl chloride in presence of aluminum chloride leads to formation of β-chlorovinyl ketones [1,2,3] whose high reactivity formed the basis of a series of methods of synthesis of heterocyclic and other compounds [4,5,6]. In this connection it seemed of interest to investigate the reaction of chlorides of sulfo acids with acetylene and vinyl chloride in presence of aluminum chloride. For investigation showed that the chlorides of aliphatic and aromatic sulfo acids do not enter into reaction either with acetylene or vinyl chloride in presence of aluminum chloride in the conditions that we had found suitable for condensation of carboxylic acid chlorides [2]. Subsequently we investigated, instead, the behavior of sulfuryl chloride in the same conditions.

When sulfuryl chloride is condensed with acetylene in presence of aluminum chloride in carbon tetrachloride solution, it is almost completely recovered unchanged; only traces are formed of a substance with a pungent odor and lachrymatory action which is apparently β-chlorovinylsulfochloride. Condensation of sulfuryl chloride with vinyl chloride gave a more definite result. The reaction was effected by passing a stream of vinyl chloride into a carbon tetrachloride solution of sulfuryl chloride to which aluminum chloride was gradually added. From the reaction mixture, after hydrolysis was isolated β,β-dichloroethylsulfochloride in 31.5% yield:

$$CH_2{=}CHCl + SO_2Cl_2 \xrightarrow{AlCl_3} CHCl_2CH_2SO_2Cl.$$

Even after prolonged passage of vinyl chloride in presence of two moles of aluminum chloride, we were unable to detect the formation of β,β,β',β'-tetrachlorodiethylsulfone; this result is fully consistent with the fact that sulfonic acid chlorides, as pointed out above, do not enter into condensation with vinyl chloride. Moreover, unlike the reaction of vinyl chloride with carboxylic acid chlorides, which proceeds with cleavage of hydrogen chloride and leads to formation of β-chlorovinyl ketone [3], in our case only addition takes place, and is not accompanied by cleavage of hydrogen chloride.

β,β-Dichloroethylsulfochloride is a heavy colorless liquid with a pungent odor, fairly stable in storage. When it is treated with aqueous-alcoholic caustic alkali, its sulfo group is esterified and one molecule of hydrogen chloride is split off to give the corresponding ester of β-chlorovinylsulfonic acid:

$$Cl_2CHCH_2SO_2Cl + ROH \xrightarrow{NaOH} ClCH{=}CHSO_2OR;\quad R = CH_3,\ C_2H_5.$$

In this way we prepared the methyl and ethyl esters. This route to previously unknown esters of β-chlorovinylsulfonic acids may serve for their preparation. The esters are colorless liquids with a faint odor, stable when kept. Treatment of β,β-dichlorovinylsulfochloride with aqueous caustic alkali gives a substance which behaves like β-chlorovinylsulfochloride. We did not isolate it in the analytically pure form; it was evidently contaminated with the original β,β-dichloroethylsulfochloride.

EXPERIMENTAL

1. β,β-Dichloroethylsulfochloride. Into a solution of 50.0 g sulfuryl chloride in 80.0 ml carbon tetrachloride, with stirring and cooling with ice water, was passed a vigorous stream of vinyl chloride (prepared from 150 g dichloroethane and a solution of 150 g KOH in 225 ml methanol [7]), and at the same time 60 g $AlCl_3$ was added in the course of an hour. After treatment with the vinyl chloride for 4-5 hours, the darkened, homogeneous mass was poured onto ice and stirred for a few minutes. The lower layer was separated, the aqueous layer was extracted with ether, the combined extracts were dried over calcium chloride, the solvent driven off and the residue distilled in vacuum to give a fraction with b.p. 89-92° at 25 mm.

After a second distillation, the β,β-dichloroethylsulfochloride had the following constants: b.p. 81-82° at 4 mm, n_D^{20} 1.5066, d_4^{20} 1.6577. Yield 23 g (31.5% of the theoretical). A heavy colorless oil with a pungent odor.

Found %: S 16.20, 16.10. $C_2H_3O_2SCl_3$. Calculated %: S 16.21.

2. Methyl ester of β-chlorovinylsulfonic acid. To a solution of 20 g β,β-dichloroethylsulfochloride in 25 ml methanol was added, with stirring, a solution of 10 g NaOH in 40 ml water at such a speed that the temperature of the mixture was maintained at 0-10°. At the conclusion of the addition of alkali, the mixture was stirred at room temperature for another 30 minutes. The lower layer was then separated and the aqueous layer extracted with ether. The extracts were washed with water and dried over sodium sulfate. The ether was distilled off and the residue distilled in vacuum to give a fraction with b.p. 89-91° at 7 mm. After a second distillation in vacuum, the methyl ester of β-chlorovinylsulfonic acid had the following constants: b.p. 90-91° at 7 mm, n_D^{20} 1.4755; d_4^{20} 1.4244. Yield 6.0 g (38% of the theoretical). Colorless mobile oil with a faint odor, insoluble in water.

Found %: C 23.01, 22.97; H 3.10, 3.17. $C_3H_5O_3SCl$. Calculated %: C 23.19, H 3.22.

3. Ethyl ester of β-chlorovinylsulfonic acid. Prepared by the above procedure from 20.0 g β,β-dichloroethylsulfochloride, 25 ml alcohol and a solution of 10 g NaOH in 40 ml water. Distillation of the reaction product in vacuum gave a fraction with b.p. 103-106° at 10 mm. After a second distillation the ethyl ester of β-chlorovinylsulfonic acid had the following constants: b.p. 96-97° at 7 mm, n_D^{20} 1.4688, d_4^{20} 1.3340. Yield 7.0 g (37%). Colorless oil with a faint odor, insoluble in water.

Found %: C 27.68, 27.71; H 4.25, 4.21. $C_4H_7O_3SCl$. Calculated %: C 28.15; H 4.14.

SUMMARY

1. Reaction of sulfuryl chloride with vinyl chloride in presence of aluminum chloride gives β,β-dichloroethylsulfochloride in 31% yield.

2. Treatment of β,β-dichloroethylsulfochloride in solution in an alcohol with aqueous alkali gives the corresponding esters of β-chlorovinylsulfonic acid.

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SULFONATION AND SULFONIC ACIDS OF ACIDOPHOBIC COMPOUNDS

XXII. THE SULFONATION OF VINYL ETHERS AND ESTERS

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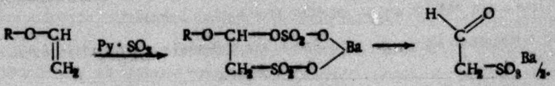
In a previous communication [1] was described the sulfonation of vinylbutyl and vinylisoamyl ethers by the action of pyridinesulfotrioxide in a medium of dichloroethane. This reaction proceeds very slowly at room temperature, but on heating to 60-80° it is completed in 6-8 hours. Hydrolysis of the reaction product in both cases was followed by isolation of a barium salt with the composition $C_2H_3O_4S^{Ba}/_2 \cdot H_2O$, which corresponds to the barium salt of acetaldehyde sulfonic acid. It was shown that an intermediate product is a salt of an alkoxyethionic acid



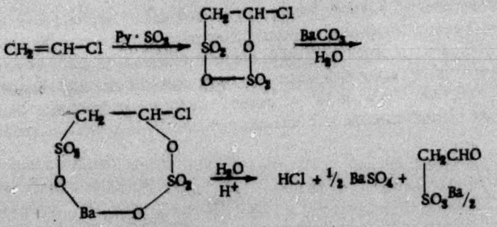
In this investigation we attempted to react pyridine- and dioxane-sulfotrioxides with a whole series of vinyl ethers and esters.

Our first aim was to improve the conditions of sulfonation of vinylbutyl ether with pyridine-sulfotrioxide, since the yield in this reaction did not exceed 30% of the theoretical.

Experiments were carried out on sulfonation in an open vessel (on the water bath under a reflux condenser); attempts were made to sulfonate at lower (30°, 16 days) and higher (150°) temperatures, also without a solvent and in presence of various inert substances. The yields, however, were of the same order (30-35%) since it was still impossible to avoid polymerization completely. We did not isolate any addition products.

Sulfonation was also carried out on vinyl chloride and isocrotyl bromide *, whose structure and properties entitle them to be regarded as vinyl esters of hydrohalogen acids. The literature contains data only for sulfonation (with oleum) of the acid-stable dichloroethylene and trichloroethylene.

In attempts to sulfonate vinyl chloride with sulfur trioxide in dichloroethane solution, we did not observe a reaction at room temperature, while heating to 50-60° resulted in instantaneous polymerization. When heated, however, with pyridine-sulfotrioxide in dichloroethane solution ($1\frac{1}{2}$-2 hours, 170°), vinyl chloride could be sulfonated. Treatment with barium carbonate and hydrolysis gave a barium salt which analyzed as barium acetaldehydesulfonate.



The greatest difficulty was here encountered in purification from the barium chloride. Silver salts proved to be inapplicable since the silver salt of acetaldehyde sulfonic acid is very poorly soluble. Again, the lead salt was, on the contrary, so hygroscopic that it could not be obtained pure.

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* L. L. Obreimova took part in the experimental work.

The problem was solved by extracting the barium chloride with hot ethyl alcohol, and the pure barium salt of acetaldehyde sulfonic acid was obtained free from water of crystallization. The purity and composition of this salt were confirmed by analysis. On recrystallization from water it formed a monohydrate. The yield proved to be very small (5% of the theoretical), and other sulfonation conditions were therefore tried with the aim of avoiding polymerization.

Attempts to sulfonate in ampoules without a solvent or in an ether medium gave even worse resinification. Sulfonation does not proceed at temperatures below 160°. Somewhat better results were got by passing vinyl chloride through a tube with pyridine-sulfotrioxide heated to 160°. In these conditions the yield reached 15%.

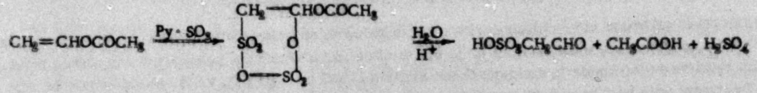
As was subsequently established, however, the low yields are due mainly to the large losses during extraction. On analysis of the unpurified salt for barium, sulfur, carbon, hydrogen and halogen, it was found that on the basis of the barium salt it contains only barium acetaldehyde sulfonate in amount corresponding to a yield of 40-[illegible]% of the theoretical. In these conditions vinyl bromide is not sulfonated because already at 130° polymerization occurs even in presence of much solvent.

Isocrotyl bromide (prepared by dehydrobromination of isobutylene bromide) sulfonates more readily than vinyl chloride. The reaction begins at only 105° and is complete after 10-15 hours without any substantial polymerization. Yield about 85% (it was not purified from barium bromide).

Turning our attention to vinyl esters, we studied the action of pyridine-sulfotrioxide on vinyl acetate * and isocrotylacetate.

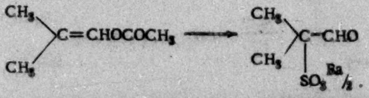
We obtained the best yield of acetaldehyde sulfonic acid by jointly heating the vinyl acetate, pyridine-sulfotrioxide and dichloroethane (solvent) in sealed ampoules for 8-10 hours at 110-120°. If the pyridine-sulfotrioxide is taken in equimolar amount, then the yield is about 85%. There is no substantial change of yield when using twice the amount of sulfonating agent. The salt obtained by the usual treatment of the reaction product contains, apparently, the barium salt of the sulfonic acid of vinyl acetate $CH_3COOCH{=}CHSO_3{}^{Ba}/_2$. The presence of this compound is confirmed by the fact that the salt solution decolorizes bromine water and permanganate, and gives off acetic acid when boiled with sulfuric acid, whereas the barium salt of the sulfonic acid of the aldehyde is stable to acids, does not decolorize bromine water and neutral permanganate solution, and turns red when boiled with caustic alkali.

With the aim of effecting smooth removal of the acetic acid, we slightly modified the method of separation of the reaction product in that the sulfonated mass was at once subjected to acidic hydrolysis, after which (after distilling off the acetic acid) the treatment with barium acetate was carried out



$$HOSO_3CH_2CHO \xrightarrow{BaCO_3} {}^{Ba}/_2\ OSO_3CH_2CHO$$

In a similar manner as for vinyl acetate, sulfonation was effected of isocrotyl acetate (prepared by heating isobutyraldehyde with acetic anhydride and potassium acetate). In this case, however, the reaction proceeds with more difficulty. After 10 hours' heating of isocrotyl acetate with pyridine-sulfotrioxide in an ampoule at 150°, considerable resinification took place and a portion of the isocrotyl acetate (about 60 %) was recovered unchanged. The yield of barium salt of α-isobutyraldehyde sulfonic acid was 35% of the theoretical, calculated on the acetate entering into reaction



We see from the above that pyridine-sulfotrioxide does not in all cases permit of good yields of aldehyde sulfonic acids. On the other hand, sulfonation of aldehydes with dioxane-sulfotrioxide gave good results [3].

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* E. E. Khaskina took part in the experimental work.

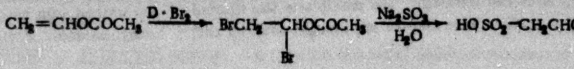
We therefore tried the action of dioxane-sulfotrioxide on some vinyl ethers. Vinylbutyl ether is sulfonated by dioxane-sulfotrioxide even at low temperature with resinification, giving a yield of only 42%. Vinyl acetate does not form resins. The yield of sulfonic acid of the aldehyde (in the form of barium salt) is 62%. In the same conditions isopropenyl acetate gave acetonesulfonic acid in 67% yield.

In the course of our study of the properties of acetaldehyde sulfonic acid, numerous experiments led to the discovery of a derivative possessing a characteristic melting point. This was the S-(β-naphthyl)-thiuronic salt (m.p. 202-204°). Applying the mixed melting point test, we demonstrated the identity between the products of sulfonation of acetaldehyde, [3], vinylbutyl ether and vinylacetate. For the purpose of obtaining a stricter proof of structure, we attempted to replace the chloromercuri-group in chloromercuriacetaldehyde by treatment with sulfur trioxide (chloromercuri)-acetaldehyde was prepared by the method of A. N. Nesmeyanov, N. F. Lutsenko and Z. M. Tumanova by the action of mercuric acetate on vinyl acetate followed by decomposition with sodium chloride [4]. It transpired, however, that in the conditions that we selected, not only substitution of the mercuri-group occurs but also oxidation of the aldehyde group. Consequently the reaction gave the barium salt of sulfoacetic acid. On acidification, this compound readily loses carbon dioxide which turns baryta water cloudy; it does not form an insoluble S-(β-naphthyl)-thiuronic salt

$$ClHgCH_2CHO \xrightarrow{2SO_3} HOSO_2CH_2COOH.$$

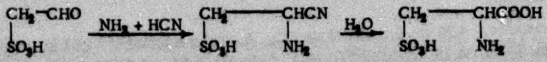
Oxidation of acetaldehyde sulfonic acid to sulfoacetic acid has been described previously [1].

On acting on vinyl acetate with dioxane dibromide (proposed for substitution of hydrogen atoms for bromine in vinyl compounds [5]), we obtained —instead of bromovinyl acetate —an addition product, i.e. dibromoethyl acetate. Treatment of this substance with excess of aqueous sodium sulfite solution gave acetaldehyde-sulfonic acid; its S-(β-naphthyl)-thiuronium salt did not give a melting point depression with the previously described specimens



$$CH_2{=}CHOCOCH_3 \xrightarrow{D\cdot Br_2} BrCH_2{-}\underset{\displaystyle Br}{\underset{|}{C}}HOCOCH_3 \xrightarrow[H_2O]{Na_2SO_3} HOSO_2{-}CH_2CHO.$$

As was observed by Schroeter [6] and others [1,3], there is a reduction of the reactivity of the aldehyde group in α-aldehyde sulfonic acids. Nevertheless it was of interest to attempt the cyanohydrin synthesis with the aim, for instance, of obtaining cysteic acid from acetaldehyde-sulfonic acid.



$$\underset{\displaystyle SO_3H}{\underset{|}{C}}H_2{-}CHO \xrightarrow{NH_3 + HCN} \underset{\displaystyle SO_3H}{\underset{|}{C}}H_2{-}\underset{\displaystyle NH_2}{\underset{|}{C}}HCN \xrightarrow{H_2O} \underset{\displaystyle SO_3H}{\underset{|}{C}}H_2{-}\underset{\displaystyle NH_2}{\underset{|}{C}}HCOOH$$

We carried out a series of experiments with barium, sodium and ammonium salts of acetaldehyde sulfonic acid. The cyanohydrin synthesis was performed by the three main methods described in the literature: Strecker's method (with hydrocyanic acid and ammonia), Lyubavin's method (with ammonium cyanide) and Zelinsky's method (with potassium cyanide and ammonium chloride). The temperature regime was also varied from room temperature to 100°. Different hydrolyzing agents were also tried out: barium hydroxide, sulfuric and hydrochloric acids. The amino acid was determined qualitatively by the ninhydrin reaction and then quantitatively by the Van Slyke and Kjeldahl methods. We did not isolate the substance in the pure state.

It transpired that the barium salt of acetaldehyde-sulfonic acid does not react with ammonium cyanide to any substantial extent even at 100° (negative or feeble reaction with ninhydrin). With ammonium cyanide the sodium salt only gives traces of amino acid (5 hours at 35°), but in Zelinsky's conditions (potassium cyanide and ammonium chloride at room temperature) it gives cysteic acid in 12.9% yield. The ammonium salt was tested out in Strecker's conditions and gave yields of 1 to 3%.

Consequently the best conditions for the cyanohydrin synthesis were those of Zelinsky; but even then the yield was low (12.9%). Determination of total nitrogen gave a similar figure (11.4%) which is within the limits of experimental error. Hence the low yield is not due to the reaction proceeding in the direction of formation of imino compounds. To confirm this, we titrated the unreacted cyanogen ion and found that only 15% of the cyanide had been consumed. The low yield is also explained by this fact. An attempt to raise the reaction temperature led to darkening of the mixture and a lowering of the yield.

It has thus been shown that it is possible in principle to perform the cyanohydrin synthesis with α-aldehyde sulfonic acids; the reaction, however, proceeds very sluggishly.

EXPERIMENTAL

Sulfonation of vinyl chloride. A mixture of 5 g (0.02 mole) 25% solution of vinyl chloride in dichloroethane and 6 g (about 0.04 mole) pyridine-sulfotrioxide was sealed into an ampoule and heated for $1^1/_2$-2 hours at 170°. The dark-brown reaction product was dissolved in water, treated with barium carbonate until neutral to Congo and then steam-distilled to remove the pyridine. The residue was filtered; the filtrate was decolorized by boiling with animal charcoal and then evaporated to a small volume; the barium salt was brought down with methyl alcohol. The solid salt was extracted with hot ethyl alcohol for 3 days (in a Soxhlet). The residue was 0.2 g barium acetaldehyde sulfonate, i.e. 5% of the theoretical yield.

8.03 mg substance: 4.918 mg $BaSO_4$. Found %: Ba 36.04. $C_2H_3O_4S^{Ba}/_2$. Calculated %: Ba 35.81.

Sulfonation of isocrotyl bromide. 0.8 g (0.006 mole) isocrotyl bromide and 4.0 g (0.025 mole) pyridine-sulfotrioxide were heated in a sealed ampoule for 6 hours at 110°. After treatment of the reaction product with barium carbonate, distilling off the pyridine, and precipitating with alcohol, there was obtained 1.8 g dry barium salt containing (on the basis of the halogen analysis) about 0.76 g barium bromide. The yield of barium salt of α-isobutyraldehyde sulfonic acid was about 85% of the theoretical. (The compound was not isolated in the pure form). The solution of the salt reduces ammoniacal silver solution and gives a coloration with fuchsine-sulfurous acid. The lead salt was obtained in the form of a thick, syrupy mass containing traces of bromine ion. The silver salt is insoluble in water.

Sulfonation of vinylbutyl ether. a) 2.0 g (0.02 mole) vinylbutyl ether, 3.2 g (0.02 mole) pyridine-sulfotrioxide and 6 ml dichloroethane were heated in a sealed ampoule for 9 hours at 70-90°. The dark mass was converted into barium acetaldehyde sulfonate by boiling on the water bath with an aqueous suspension of barium carbonate until the pyridine had gone off. The precipitate was filtered off and washed with hot water; the filtrate was evaporated to a small volume and the salt brought down by adding methyl alcohol. Yield 2.6 g or 30% of the theoretical.

7.907 mg substance: 5.415 mg $BaSO_4$. 7.832 mg substance: 4.763 mg $BaSO_4$. Found %: Ba 35.79, 35.92. $C_2H_3O_4S^{Ba}/_2$. Calculated %: Ba 35.81.

If the salt is prepared by evaporating the aqueous solution, the barium salt is obtained with one molecule of water of crystallization.

0.0970 g substance: 4.82 ml 0.09988 N Na_2CO_3. 0.0920 g substance: 4.58 ml 0.09988 N Na_2CO_3. Found %: Ba 34.10, 34.15. $C_2H_3O_4S^{Ba}/_2 \cdot H_2O$. Calculated %: Ba 34.34.

b) A mixture of 4.0 g (0.04 mole) vinylbutyl ether, 13 g (0.08 mole) pyridine-sulfotrioxide and 40 ml dichloroethane was refluxed in a round-bottomed flask for 14 hours on a water bath. The sulfonated mass was worked up as in the preceding experiment. Yield of barium acetaldehyde sulfonate 5.6 g or 32.5% of the theoretical.

c) A solution of 4.0 g (0.05 mole) sulfur trioxide in 25 ml dichloroethane was cooled to 0°; to it was added 4.4 g (0.1 mole) dioxane, and to the resultant solution of dioxane-sulfotrioxide was added 2.5 g (0.025 mole) vinylbutyl ether. The mixture was left for 6 hours and then decomposed with water and evaporated on the water bath for 4 hours for removal of solvent and butyl alcohol. The residue was treated with barium carbonate and the filtrate evaporated and barium acetaldehyde sulfonate precipitated by adding methyl alcohol. Yield 2.0 g (42% of theory).

Preparation of S-β-naphthyl-thiuronic salt of acetaldehyde sulfonic acid. To a cooled saturated solution of S-(β-naphthyl)-thiuronyl chloride was added a saturated aqueous solution of the barium salt of sulfoacetaldehyde. A flocculent precipitate formed immediately and was filtered off, dried in vacuum over phosphorus pentoxide and recrystallized from absolute benzene. Colorless crystals with m.p. 202-204°.

Sulfonation of vinyl acetate.

a) A mixture of 2.3 g (0.03 mole) vinyl acetate (b.p. 72-74° at 760 mm; n_D^{20} 1.3958), 5.0 g (0.03 mole) pyridine-sulfotrioxide and 10 ml dichloroethane was heated in an ampoule for 8 hours at 120°. The sulfonated mass was dissolved in hot water; 0.5 ml 0.2 N sulfuric acid was added before boiling for 4 hours; the acetic acid was distilled off in steam. The residue was treated with barium carbonate and the pyridine distilled off in steam. The precipitate was filtered and washed with hot water. The filtrate was evaporated down and the barium acetaldehydesulfonate was precipitated by addition of methyl alcohol. Yield 4.4 g or 85% of the theoretical.

0.0962 g substance: 5.07 ml 0.09988 N Na_2CO_3. 0.0990 g substance: 5.40 ml 0.09988 N Na_2CO_3. Found %: Ba 36.15, 36.21. $C_2H_3O_4S^{Ba}/_2$. Calculated %: Ba 35.81.

b) A solution of 8 g (0.1 mole) sulfur trioxide in 50 ml dichloroethane was cooled to 0°, 8.8 g (0.2 mole) dioxane was added, followed (with stirring) by 4.3 g (0.05 mole) vinyl acetate. The mixture was left for 6 hours, poured into cold water and evaporated for 8 hours on the water bath with two additions of 5 ml water each. The mass was then treated with excess barium carbonate, the precipitate filtered off, and the filtrate evaporated until crystallization started. Cooling brought down 6.5 g of the barium acetaldehyde sulfonate containing one molecule of water of crystallization. Yield 62% of the theoretical. The S-(β-naphthyl)-thiuronic salt had m.p. 202-204°. No depression of m.p. in mixed melting test with the salt prepared from vinylbutyl ether.

Sulfonation of isopropenyl acetate. To an ice-cooled solution of 1.0 g (0.013 mole) sulfur trioxide in 6 ml dichloroethane was added, with stirring, 0.9 g (0.01 mole) dioxane, followed by 1.0 g (0.01 mole) isopropenyl acetate. Working-up in the usual manner gave 1.5 g of the monohydrate of the barium salt of acetonesulfonic acid. Yield 67% of the theoretical.

0.0579 g substance: 0.0306 g $BaSO_4$. 0.0177 g substance: 0.0093 g $BaSO_4$. Found %: Ba 31.05, 30.80. $C_3H_5O_4S^{Ba}/_2 \cdot H_2O$. Calculated %: Ba 30.66.

Preparation of isocrotyl acetate. A mixture of 28.8 g (0.4 mole) isobutyraldehyde, 61 g (0.6 mole) distilled acetic anhydride and 6 g (0.06 mole) potassium acetate was heated for 10 hours on an oil bath under a condenser. The mass was then poured on to ice and the seperated layer was washed with ice water and with sodium bicarbonate solution. After drying over magnesium sulfate, the substance was distilled in a dephlegmator, giving 36.5 g isocrotyl acetate or 80% of the theoretical yield. B.p. 121-124° at 756 mm; n_D^{20} 1.4106 in agreement with the literature.

Sulfonation of isocrotyl acetate. 3 g (about 0.025 mole) isocrotyl acetate and 8 g (0.05 mole) pyridine-sulfotrioxide were sealed into an ampoule and heated for 10 hours at 150°. From the thick, partly polymerized mass was distilled off 2.0 g nonreacted isocrotyl acetate. The residue was treated with barium carbonate, the pyridine distilled off in steam. The usual method of working-up gave 0.59 g barium salt of α-isobutyraldehyde sulfonic acid, i.e. 35 % of the theoretical yield, calculated on the isocrotyl acetate entering into reaction.

5.615 mg substance: 3.044 mg $BaSO_4$. 4.331 mg substance: 2.338 mg $BaSO_4$. Found %: Ba 31.90, 31.78. $C_4H_7O_4S^{Ba}/_2$. Calculated %: Ba 31.25.

Action of sulfur trioxide on (chloromercuri)acetaldehyde. In a small flask fitted with a reflux condenser was placed 1.4 g (0.005 mole) (chloromercuri)-acetaldehyde [4], and a solution of 2.0 g (0.025 mole) sulfur trioxide in 30 ml dichloroethane was run in with cooling. The mixture was then heated for 12 hours on the water bath, 10 ml water was added, the dichloroethane was evaporated off on the water bath and the mercury salts were precipitated with hydrogen sulfide. The filtered solution was treated with barium carbonate, filtered, washed three times with boiling water and again evaporated. The poorly soluble salt of sulfoacetic acid was recrystallized from water. Yield 0.6 g (41% of theory) of the monohydrate of the barium salt of sulfoacetic acid.

0.0094 g substance: 0.0075 g $BaSO_4$. Found %: Ba 46.45. $C_2H_2O_5SBa \cdot H_2O$. Calculated %: Ba 46.79.

Reaction of dioxane dibromide with vinyl acetate. To 21.2 g (0.25 mole) vinyl acetate was added, in small portions with cooling, 62 g (0.25 mole) dioxane dibromide [5]. Each portion of the dioxane dibromide quickly dissolved on addition, imparting to the reaction mixture the characteristic color of bromine which quickly disappeared, however (in 1-2 minutes). After the end of the reaction, the layers were separated. The lower layer was washed with ice water, dried with calcium chloride and distilled in vacuum to give 31.2 g dibromide (50% of the theoretical). Dibromoethyl acetate is a colorless oil with a strong odor of radish. It is lachrymatory. B.p. 101-103°, at 32 mm; n_D^{20} 1.5057; d_4^{20} 1.9170; MR_D 38.24, calculated 37.85.

Literature data: b.p. 84-85° at 5 mm; n_D^{20} 1.5052; d_4^{20} 1.9185 [7].

8.260 mg substance: 5.955 mg CO_2; 1.820 mg H_2O; 5.365 mg Br_2. Found %: C 19.67; H 2.47; Br 64.95. $C_4H_6O_2Br_2$. Calculated %: C 19.54; H 2.46; Br 64.98.

Reaction of dibromoethyl acetate with sodium sulfite. To a solution of 3.0 g (0.025 mole) pure sodium sulfite in 25 ml water was added 2.5 g (0.01 mole) dibromoethyl acetate and the mixture was heated under a reflux condenser. After an hour the mixture had become homogeneous. The light-yellow solution was evaporated, treated with barium carbonate, filtered and again evaporated. The cooled concentrated solution of barium acetaldehyde sulfonate was added to a cooled saturated solution of S-(β-naphthyl)-thiuron chloride. The immediately formed precipitate was filtered, washed with water, dried in a vacuum-desiccator and recrystallized from absolute benzene. M.p. 202-203°. A mixed melting test with the S-(β-naphthyl)-thiuronic salt of acetaldehydesulfonic acid prepared from vinyl acetate or from acetaldehyde [3] did not give a depression.

Cyanohydrin synthesis with acetaldehyde sulfonic acid. a) A mixture of 1.0 g (0.005 mole) barium salt of acetaldehyde sulfonic acid and 10 ml (0.007 mole) 3.15% aqueous solution of ammonium cyanide [8] was heated in a sealed ampoule for 5 hours at 60° and then stood for two days at room temperature. Addition was then made of 7 ml concentrated sulfuric acid; the mixture was refluxed for 12 hours, neutralized hot with barium carbonate and filtered. The precipitate was washed with hot water and the combined filtrates were evaporated down on a water bath. The residue gave a weak positive ninhydrin reaction.

b) To a solution (2 ml) of ammonium acetaldehyde sulfonate (prepared from 1.0 g barium salt by treatment with ammonium sulfate) was added 0.3 ml anhydrous hydrocyanic acid. The mixture was stood for 24 hours at room temperature. Then a stream of ammonia was passed through it with ice cooling for an hour; the mass was again left for 24 hours. The reaction mixture was then hydrolyzed with hydrochloric acid and worked up as in the preceding experiment. The ninhydrin test was positive. Van Slyke ammonia determination: 2 ml substance: 0.33 ml N_2 (20°, 742 mm). Total amount of solution 23 ml. Yield of amino acid (calculated on the aldehyde) 3.02%.

c) To a mixture of 0.75 g (0.005 mole) sodium acetaldehyde sulfonate, 0.3 g (0.057 mole) ammonium chloride and 0.4 g (0.057 mole) 92% KCN was added a few drops of water and the mass kept at room temperature for 48 hours with periodic shaking. Addition was then made of an equal amount of concentrated acid, and the mixture stood for 12 hours at room temperature, diluted with double the amount of water and refluxed for 7 hours. The hydrolyzate was then evaporated to dryness on the water bath. To the dry residue was added a concentrated solution of sodium hydroxide and the ammonia was distilled off; the liquid was then transferred to a measuring flask, made up to the mark and analyzed for nitrogen content.

The yield of amino nitrogen was found to be 12.9%, calculated on the aldehyde, and 11.4% on the basis of nitrogen volume, which is within the limits of analytical error.

SUMMARY

1. Reaction of sulfur trioxide in complex form (pyridine-sulfotrioxide or dioxane-sulfotrioxide) with vinyl chloride, isocrotyl bromide, vinylbutyl ether, vinyl acetate, isopropenyl acetate and isocrotyl acetate gave the corresponding α-aldehyde sulfonic acids or α-sulfoketones, as was established by analyses and by other syntheses of acetaldehyde sulfonic acid.

2. Reaction of (chloromercuri) acetaldehyde with sulfur trioxide leads to substitution of the mercuric group by the sulfo group with simultaneous oxidation to sulfoacetic acid.

3. In the reaction of dioxane-sulfotrioxide with vinyl acetate, the hydrogen atom is not substituted, but instead a molecule of bromine adds on at the double carbon-carbon bond.

4. Heating of α, β-dibromoethyl acetate with an aqueous solution of sodium sulfite converts the former into acetaldehyde sulfonic acid.

5. The possibility of preparing α-amino-β-sulfo acids by the cyanohydrin synthesis from α-aldehyde-sulfonic acids is demonstrated.

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SYNTHESES WITH ACRYLONITRILE

XIX. REDUCTION OF ACRYLONITRILE BY VYSHNEGRADSKY'S METHOD

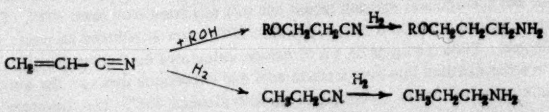
V. G. Yashunsky, A. N. Kost, and A. P. Terentyev

A. N. Kost and V. G. Yashunsky have previously shown [1] that in the reduction of β-substituted propionitriles ($R-X-CH_2CH_2CN$) with sodium in alcohol, the R–X group is replaced by the alkoxy group of the alcohol in which the reduction is carried out. A mechanism was proposed for this reaction which involved intermediate formation of acrylonitrile and its addition to the alcohol to form the β-alkoxy-propionitrile which underwent reduction to the γ-alkoxypropylamines.

For the purpose of establishing the above mechanism of anomalous reduction of β-substituted propionitriles we carried out the reduction of acrylonitrile itself. The literature only contains details of its catalytic hydrogenation [2]. It has also been shown [3] that acrylonitrile is converted into adiponitrile by the action of magnesium amalgam in a methyl alcohol medium. We reduced acrylonitrile with sodium in ethyl, butyl, isobutyl and isoamyl alcohols. The main products that we isolated were, as anticipated, the corresponding γ-alkoxypropylamines. The lowest yield of alkoxyamine was obtained with ethyl alcohol (30% calculated on the acrylonitrile); reduction in butyl alcohol gave 44.3% of amine, and in isoamyl alcohol 41.4%. The yield of alkoxyamines is considerably increased by working with large quantities ($1^1/_2$ times more than usual) of sodium and alcohol; thus, γ-butoxypropylamine and γ-isobutoxypropylamine were obtained in yields of 59.6 and 63% respectively. Moreover, it was found that increased yields of alkoxyamine can be achieved by running the alcoholic solution of acrylonitrile into the sodium under toluene.

All the reductions of acrylonitrile gave small amounts (up to 13% calculated on the acrylonitrile) of propylamines which were isolated as the hydrochlorides. We have published a short communication on these experiments [4].

The preferential formation of γ-alkoxypropylamines is explained by the fact that in these conditions the most active portion of the acrylonitrile molecule is the double carbon-carbon bond, and therefore competition arises between the reaction of alcohol addition and the reaction of hydrogen addition.



In our conditions the velocity of the first reaction predominates considerably. The large amount of alcohol in which the reduction took place (molar ratio of acrylonitrile to alcohol = 1:45) also promoted the first reaction. The meager literature data about the reduction of nitriles of unsaturated acids by Vyshnegradsky's method indicate that if the double bond is remote from the nitrile group, then reduction leads to the corresponding unsaturated amine [5]. But when the nitrile group is directly located at the double bond, then the latter is hydrogenated with formation of the saturated base although yields of amines rarely reach 20% [6,7] and, indeed, in the majority of cases only traces of amines can be isolated. The main products of reduction of such nitriles are hydrocarbons. Thus, Freund [6] reduced α-phenylcinnamonitrile and isolated β, γ-diphenylpropylamine and dibenzyl; the amount of the latter was more than 4 times greater than that of the amine. In the case of cinnamonitrile not even traces of γ-phenylpropylamine could be detected in the end products.

Consequently, if the nitrile group is conjugated with the double bond, then in the conditions of Vyshnegradsky's reaction the reduction of this double bond is inhibited. The result of this is that other reactions can proceed which are facilitated by the presence of the polar CN group.

In our case such a reaction was the addition of an alcohol. In the case of nitriles of cinnamic acids, the formation of alkoxynitriles is evidently hindered by the presence in the β-position of a phenyl radical, and here the reactions proceed in another direction (in the main with cleavage of the nitrile group).

The formation of γ-alkoxypropylamines as the main products of reduction of acrylonitrile by sodium in alcohols is consequently accounted for by the peculiarity of the structure of this molecule which permits reciprocal influence between the CN group and the carbon-carbon double bond.

The preparation of γ-alkoxypropylamines by reduction of acrylonitrile (Vyshnegradsky's method) proved to be a convenient preparative method. For example, for the synthesis of γ-ethoxypropylamine, Utermohlen [8] first performed cyanoethylation of ethyl alcohol (yield 78%) and then catalytic hydrogenation of the obtained nitrile (yield 50%), i.e. the total yield of amine (calculated on the acrylonitrile) was 39%. In the case of γ-butoxypropylamine it was 61%. In our procedure the amine yields are of a similar order but the final products are obtained in one step without separation of intermediate products.

EXPERIMENTAL

Preparation of γ-Ethoxypropylamine

To a boiling solution of 5.3 g (0.1 mole) acrylonitrile in 130 ml absolute alcohol, placed in a two-necked liter flask fitted with a high-capacity reflux condenser, was added 15 g sodium over a period of 20 minutes. After the metal had gone into solution, addition was made to the alcoholic solution of about 100 ml water, and the mixture was steam-distilled for many hours. The distillate was collected in a receiver containing 10% hydrochloric acid. A purer product was obtained by bubbling steam through the hydrochloric acid solution and then evaporating this solution on the water bath. The residue – a thick, yellow oil – was decomposed with solid NaOH under a layer of ether and repeatedly extracted with absolute ether. The ethereal solution was dried with fused KOH, the ether was distilled off, and the base twice distilled in vacuum.

There was obtained 3.0 g γ-ethoxypropylamine (yield 30% calculated on the acrylonitrile). B.p. 49-50° at 30 mm.

Preparation of γ-Isobutoxypropylamine

Into 50 ml hot toluene containing 22 g sodium * was run a solution 5.3 g (0.1 mole) acrylonitrile in 350 ml absolute isobutyl alcohol over a period of 30 minutes. Throughout the whole of the reaction period the flask was heated on an oil bath at a temperature of 140-150°. After the whole of the sodium had dissolved, 200 ml water was added and the mixture distilled with steam. The distillate was collected in dilute hydrochloric acid; after checking that the solution was acid to Congo, the alcoholic layer was separated and the isobutyl alcohol distilled off with steam. The residue from the distillation was combined with the aqueous layer from the first distillate and evaporated on the water bath. The γ-isobutoxypropylamine hydrochloride was decomposed with powdered NaOH under a layer of ether, the base was extracted with ether, and the ethereal solution (about 300 ml) was dried with fused KOH. The ether was distilled into dilute hydrochloric acid and the residue distilled in a dephlegmator at reduced pressure. A fraction boiling at 72-73° (34 mm) was collected. Yield 8.27 g or 63.1% of theory, calculated on the acrylonitrile. The aqueous layer was separated from the ether, distilled into hydrochloric acid and evaporated down on the water bath to give 1.28 g white crystals of propylamine hydrochloride. M.p. (from aqueous alcohol) 156°. The literature [9] gives m.p. 157-158°.

Reduction by a similar method of acrylonitrile in n-butyl alcohol (5.3 g acrylonitrile, 15 g sodium and 220 ml of the alcohol) gave γ-butoxypropylamine in 44.3% yield. B.p. 78-79° at 23mm. On using the same quantities of sodium and alcohol for reduction of 3.2 g (0.066 mole) acrylonitrile, the yield could be increased to 59.6%; b.p. 71-72° at 19 mm.

γ-Isoamyloxypropylamine was isolated from the products of reduction of acrylonitrile with sodium in isoamyl alcohol. Yield 41.4%, b.p. 78.5-80° at 18 mm.

The properties and constants of the alkoxypropylamines obtained by reduction of acrylonitrile correspond entirely to the properties and constants of the amines prepared previously by us [1]. The mixed melting points of the picrates were not depressed.

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* The amounts of sodium and alcohol used were 1 1/2 times as much as those usually taken for the reduction process.

SUMMARY

1. For the first time the reduction of acrylonitrile was effected by Vyshnegradsky's method (sodium in various alcohols).

2. It was shown that in this reaction the alcohol undergoes cyanoethylation and this is followed by reduction of the nitrile group. The main product of the reaction in 30-60% yield is γ-alkoxypropylamine; only an insignificant amount of isopropylamine is formed.

3. The method can serve as a preparative method for γ-alkoxypropylamines.

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* See Consultants Bureau English Translation, p. 239.

THE REACTION OF ALDEHYDES AND KETONES WITH ACETIC ANHYDRIDE

III. REACTION OF CYCLOPENTANONE, ACETONE AND METHYLPROPYL KETONE WITH ACETIC ANHYDRIDE

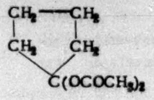
I. V. Machinskaya, V. A. Barkhash and V. I. Molchanov

In previous communications one of us showed that cyclohexanone [1] and its homologs [2] react with acetic anhydride in presence of small amounts of concentrated sulfuric acid at room temperature to form enol acetates; in short-period reaction the enol acetates are accompanied by diacetates of hydrated forms of the ketones.

In this paper we describe the reaction with acetic anhydride, in the same conditions, of cyclopentanone and of some aliphatic ketones.

Cyclopentanone was reacted with acetic anhydride in the same conditions as for cyclohexanone [1].

The data show that cyclopentanone appears to react with acetic anhydride with formation of the enol-acetate, as evidenced by decolorization of bromine water; the enol acetate, however, appears to be unstable and during distillation it partly undergoes cleavage with formation of the original ketone (the distilled fractions always gave a precipitate with bisulfite and had a strong acid reaction to litmus) *. Of the expected reaction products we only succeeded in isolating the previously undescribed diacetate of the hydrate form of cyclopentanone (I); a crystalline product with m.p. 37-39°.


(I)

On comparing our previous results for the reaction of cyclohexanone [1] and its homologs [2] with acetic anhydride with the present results for cyclopentanone, we can conclude that the formation of the acetate of the enol form proceeds more readily in the case of cyclohexanone and its homologs. This conclusion is in harmony with the data of Mousseron and Winternitz [4], of Wallach [5] and of certain other investigators who drew attention to the great tendency to double-bond formation in the cyclohexanone ring in comparison with the cyclopentanone ring.** Mousseron and Winternitz [4] arrived at this conclusion on the basis of stereochemical considerations and of a series of experimental facts. Wallach [5] established that the reaction of acetone with cyclohexanone and its homologs in presence of sodium alcoholate leads to formation of condensation products with a double bond in the ring, whereas with cyclopentanone the condensation products contain a hemicyclic double bond.

We used acetone and methylpropyl ketone in this investigation as representatives of aliphatic ketones.

Previous attempts to prepare the enol acetate by reaction of acetone with acetic anhydride had been made by Mannich [6] and Hancu [7]. In both cases, however, negative results were obtained***; mesityl oxide was isolated from the reaction mixture. Formation of mesityl oxide was also observed [9] when acetone was heated with acetic anhydride in presence of p-toluenesulfonic acid.

We have established that the reaction of acetone with acetic anhydride at room temperature in presence of a small amount of sulfuric acid gives a liquid product with b.p. 49.5-50° at 7 mm. The elementary analysis, the saponification value and the molecular refraction correspond to the diacetate of the hydrate form of acetone $(CH_3)_2C(OCOCH_3)_2$, which has not previously been described in the literature. The enol acetate of acetone, reported in the literature to have b.p. 90-96.5° [8] was not detected in the reaction products.

Reaction of methylpropyl ketone with acetic anhydride led to a product with a pleasant ethereal odor, b.p. 22.5-23.5° at 4 mm. Its elementary analysis, saponification value and molecular refraction correspond to the acetate of the enol form of methylpropyl ketone. One of the two following formulas is possible for the prepared compound:

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* It must be pointed out that the enol acetate of cyclopentanone can be prepared and isolated if the reaction is carried out in other conditions. Thus, Mannich and Hancu [3] obtained it, although in very small yield, by heating cyclopentanone with acetic anhydride at 180°.

** For the literature on this problem see the paper of Mousseron and Winternitz [4].

*** Acetone enol acetate has been prepared by another route [8].

$$\underset{\text{(II)}}{CH_3-C(OCOCH_3)=CH-CH_2CH_3}; \quad \underset{\text{(III)}}{CH_2=C(OCOCH_3)-CH_2CH_2CH_3}.$$

Formula (II) is more probable; this represents the enol acetate formed as a result of enolization of the methyl group. Thus, Hancu [7] obtained the enol acetates of diethyl- and dipropyl ketones by heating the corresponding ketones with acetic anhydride in presence of sodium acetate; in the case of acetone, however, the enol acetate was not obtained, but mesityl oxide. Bedukian [9] obtained the enol acetates of ketones by heating ketones with acetic anhydride in presence of p-toluenesulfonic acid; he established that in his experimental conditions enolization proceeded at the expense of the methylene and not of the methyl group. We failed to detect the diacetate of the hydrate form of methylpropyl ketone in the products of this reaction.

Consequently, ketones of the aliphatic series in the investigated conditions enter into reaction with acetic anhydride with formation of the diacetates of their hydrate form (acetone) or of the enol acetates (methylpropyl ketone).

In the conditions of this reaction an investigation was also made of the behavior of an aliphatic-aromatic ketone (acetophenone) and of a purely aromatic ketone (benzophenone). We established that acetophenone does not enter into reaction with acetic anhydride; it was almost completely recovered unchanged from the reaction mixture together with an insignificant amount of high-boiling fractions which were probably autocondensation products of acetophenone. Benzophenone likewise does not react with acetic anhydride, not even when heated to a temperature of 100°.

EXPERIMENTAL

1. Reaction of Cyclopentanone with Acetic Anhydride

To a mixture of 28 g freshly distilled cyclopentanone (b.p. 128-130°) and 102 g acetic anhydride (also freshly distilled —b.p. 137-140°) was added 0.26 ml concentrated sulfuric acid; slight heat was developed. The mixture was left for 5 days at room temperature. The red-colored mass was then treated with ice water for decomposition of the unreacted acetic anhydride and then extracted with ether. The aqueous layer was neutralized with sodium carbonate and again extracted with ether. The combined ether extracts were washed with sodium carbonate solution until neutral, then with water, and dried with sodium sulfate. The ether was distilled off and the residue distilled in vacuum (4 mm).

By distillation, however, we failed to isolate any constant-boiling fraction whatever: the product boiled with constantly increasing temperature from 23 to 75°. A 72-74° fraction, obtained in small amount, crystallized on standing; after two recrystallizations from moderately heated dilute alcohol, the crystals had m.p. 37-39°.

7.49 mg substance: 16.00 mg CO_2; 5.22 mg H_2O. 5.09 mg substance: 10.91 mg CO_2; 3.58 mg H_2O. Found %: C 58.30, 58.49; H 7.80, 7.87. $C_9H_{14}O_4$. Calculated %: C 58.05; H 7.58. Saponification value 608; calculated 603.

A second distillation of the reaction products likewise did not lead to isolation of the enol acetate; a series of new fractions with lower boiling points was obtained; they decolorized bromine water, had a strongly acid reaction and a high saponification value. Thus, the fraction with b.p. 25-30° at 4 mm had saponification value 246 (calculated for the enol acetate of cyclopentanone 445).

When the reaction was conducted over a longer period of time (21 days or 30 days), we again failed to isolate the enol acetate in the pure form; however, when the fractions boiling at 23-26° at 4 mm had been purified with bisulfite solution, they gave closer analytical results (for example, saponification value 402). Potassium permanganate oxidation of a bisulfite-purified fraction gave glutaric acid. The diacetate of the hydrate form of cyclopentanone was obtained in small amounts in all the experiments.

2. Reaction of Acetone with Acetic Anhydride

To a mixture of 23 g acetone, purified through the bisulfite compound (b.p. 55-56°), and 123 g acetic anhydride (b.p. 137-140°) was added 0.42 ml concentrated sulfuric acid. Slight heat was developed. The mixture was left for 13 days at room temperature and acquired a reddish-brown color. The reaction mass was worked up as in the experiment with cyclopentanone. The residue from the ether distillation was subjected to vacuum distillation, the main bulk coming over at 42-43° at 4 mm and a second distillation giving a small fraction with b.p. 49.5-60° at 7 mm. The product did not decolorize bromine water and was acid to litmus.

4.30 mg substance: 8.22 mg CO_2; 2.94 mg H_2O. 3.59 mg substance: 6.89 mg CO_2; 2.47 mg H_2O. Found %: C 52.17, 52.37; H 7.65; 7.70. $C_7H_{12}O_4$. Calculated %: C 52.49; H 7.55. Saponification value 676; calculated 700.

8. Reaction of Methylpropyl Ketone with Acetic Anhydride

To a mixture of 28.7 g methylpropyl ketone, purified through the bisulfite compound (b.p. 100-102°), and 102 g acetic anhydride (b.p. 138-140°) was added 0.26 ml concentrated sulfuric acid drop by drop. The mixture was left for 13 days, at the end of which period it had acquired a reddish-brown color. The reaction mixture was worked up in the usual manner. In view of the fact that a sample of the residue after removal of the ether gave a small precipitate when shaken with bisulfite, the whole mass was treated with bisulfite to eliminate the ketone that had not reacted (a total of 2.5 g bisulfite compound was separated). After removal of the ketone, the mixture was worked up in the usual manner. The residue after ether removal was subjected to vacuum distillation, the main bulk (9.5 g) coming over at 24-26° (6 mm); it decolorized bromine water, did not form a precipitate with bisulfite and was neutral to litmus. A second vacuum distillation gave a product with b.p. 22.5-23.5° (4 mm) with an ethereal odor; n_D^{20} 1.4178; d^{20} 0.9043; MR_D 35.70; calculated 35.71.

4.60 mg substance: 11.03 mg CO_2; 3.82 mg H_2O. 6.19 mg substance: 14.87 mg CO_2; 5.09 mg H_2O. Found %: C 65.44, 65.56; H 9.29, 9.20. $C_7H_{12}O_2$. Calculated %: C 65.60; H 9.44. Saponification value 421; calculated 438.

It should be pointed out that the methylpropyl ketone enol acetate that we obtained differs from the enol acetates of other ketones previously prepared by us in that it boils in a narrow temperature interval and has a neutral reaction; the enol acetates of cyclohexanone and its homologs always had an acid reaction and distilled over a fairly wide temperature range.

The residue from the distillation of methylpropyl ketone enol acetate (a very small amount of resinous substances) did not have an odor of acetic anhydride, as had been the case in other reactions in which the diacetates of the hydrate forms had been formed (cyclohexanone and its homologs).

SUMMARY

1. It was established that the reaction of acetic anhydride with cyclopentanone at room temperature in presence of a small amount of concentrated sulfuric acid gave, among other products, the diacetate of the hydrate form of cyclopentanone, not previously described in the literature.

2. In similar conditions acetone forms the diacetate of the hydrate form of acetone, not previously described in the literature. Methylpropyl ketone reacts in the same conditions with formation of the enol acetate.

3. Acetophenone and benzophenone do not enter into reaction with acetic anhydride in these conditions.

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SYNTHESIS OF α-HALO KETONES OF THE ACETYLENE SERIES

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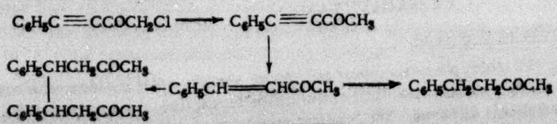
Ketones of the acetylenic series containing a triple bond conjugated with the carbonyl group were first prepared by Nef [1] and later investigated by Moureau [2,3], Andre [4] and others. More recently a method has been developed for the synthesis of the simplest representatives of this series (ethinyl ketones) and some of their chemical transformations have been studied [5]. Compounds of this type, possessing the conjugated system $-C\equiv C-\underset{|}{C}=O$, are distinguished by high reactivity and serve as starting materials for a number of syntheses. Up to now ketones of the acetylenic series containing other functional groups have been unknown. And it is evident that the presence of such groups considerably broadens the range of transformations of these compounds and provides great opportunities for their utilization for synthetic purposes.

This investigation is concerned with the synthesis of ketones of the acetylenic series containing a halogen atom in the α-position to the carbonyl group. It was thought that the synthesis of these compounds could be realized by reacting the sodium derivative of the acetylenic hydrocarbon with the acid chloride of the α-halo acid in accordance with the scheme:

$$RC\equiv CNa + XCOCHXR' \longrightarrow RC\equiv CCOCHXR'.$$

It could be assumed that only the halogen of the acid chloride grouping would enter into the reaction. Such a reaction course is consistent with the reports in the literature about the behavior of metallic derivatives of acetylenic hydrocarbons which readily react with acid chlorides [1,2,3,4] and are alkylated with great difficulty by the action of alkyl halides in a medium of nonpolar solvents [6].

We investigated the preparation of α-halo ketones of the acetylenic series with reference to the reaction of the sodium derivative of phenylacetylene with chloroacetyl chloride. From the reaction mixture was isolated a crystalline substance with the composition $C_{10}H_7OCl$, m.p. 37°, containing halogen, giving a reaction for a multiple bond and a carbonyl group. The structure of this compound was established by reduction with zinc dust in alcohol with addition of acetic acid. Reduction with excess of zinc dust gave benzylacetone (identified in the form of its semicarbazone) and a crystalline substance with m.p. 160-161°, which proved to be identical with the 4,5-diphenyloctanediol-2,7 prepared by Harries and Eschenbach [7] by reduction of benzalacetone with aluminum amalgam. Reduction with a molar equivalent of zinc dust gave a 52% yield of phenylethinylmethyl ketone, which was identified by its dinitrophenylhydrazone and by conversion into phenylmethylpyrazolone. In this case, therefore, the triple bond remains intact on reduction, so that we have direct evidence of the structure of the prepared compound. Consequently the condensation of sodium phenylacetylide with chloroacetyl chloride proceeds according to the above scheme and leads to 1-phenyl-4-chlorobutyne-1-one-3, whose reduction may be represented by the following equation:



$$\begin{tikzcd}
C_6H_5C\equiv CCOCH_2Cl \arrow[r] & C_6H_5C\equiv CCOCH_3 \arrow[d] & \\
\begin{array}{c} C_6H_5CHCH_2COCH_3 \\ | \\ C_6H_5CHCH_2COCH_3 \end{array} & C_6H_5CH=CHCOCH_3 \arrow[l] \arrow[r] & C_6H_5CH_2CH_2COCH_3
\end{tikzcd}$$

Other acid chlorides of α-halo acids react with sodium phenylacetylide in a similar manner to chloroacetyl chloride. We performed this reaction with the acid bromides of α-bromopropionic, α-bromobutyric and α-bromoisobutyric acids, and we obtained, respectively, 1-phenyl-4-bromopentyne-1-one-3, 1-phenyl-4-bromohexyne-1-one-3 and 1-phenyl-4-bromomethylpentyne-1-one-3.

The reaction is carried out by adding an ethereal suspension of sodium phenylacetylide to the acid chloride; it proceeds rather violently and is complete after a few hours. In all cases a portion of the phenylacetylene is recovered unchanged even when using a considerable excess of acid chloride. The yields of acetylenic ketones are about 40% on the average and fall slightly with increasing size of alkyl radical. Data for the compounds prepared appear in the table.

Halo ketones of the acetylenic series

Name	Yield (%)	B.p. (7 mm)	d_4^{20}	n_D^{20}	MR$_D$ Found	MR$_D$ Calc.	EMR$_D$	M.p. of the 2,4-dinitrophenylhydrazone
1-Phenyl-4-chlorobutyne-1-one-3 (m.p. 37°)	42.5	135-137°	–	–	–	–	–	170-171°
1-Phenyl-4-bromopentyne-1-one-3	47	145-146	1.3668	1.6008	59.36	55.48	3.88	188.5-189
1-Phenyl-4-bromohexyne-1-one-3	37	167.5-168.5	1.3155	1.5880	64.16	60.09	4.07	163-164
1-Phenyl-4-bromo-4-methylpentyne-1-one-3	36	146-148	1.3037	1.5843	64.43	60.09	4.34	173.5-174

As we see from the table, the prepared α-halo ketones are distinguished by a fairly high exaltation of molecular refraction. It is interesting to note that the magnitude of this exaltation is approximately greater by 0.6-0.7 than the exaltation of the corresponding acetylenic ketones not containing a halogen atom [4]. This difference corresponds exactly to the magnitude of the exaltation characteristic of the simplest α-halo ketones (chloroacetone, bromoacetone). Consequently, in our case the exaltation of molecular refraction is composed of the exaltation characteristic of the system $-C\equiv C-\underset{|}{C}=O$, and the exaltation of the system $-COCH_2X$.

All the prepared compounds manifest unsaturation: they decolorize permanganate and bromine water. They readily form derivatives at the carbonyl group; the 2,4-dinitrophenylhydrazones were selected for purposes of characterization since, as far as we are aware, they have the least tendency to form cyclic derivatives due to secondary transformations.

The prepared acetylenic α-halo ketones are characterized by sensitivity to alkaline agents. Alcoholic and aqueous solutions of caustic alkalies in the cold and sodium carbonate solution at higher temperatures bring about almost complete resinification of the halo ketone. The same change occurs when the halo ketone is boiled with an aqueous suspension of barium carbonate. This behavior is undoubtedly associated with the lability of the halogen which, as we know from the work of A. E. Favorsky, S. N. Danilov and others, is characteristic of α-halo ketones in general; in our case the lability of the whole system increases markedly due to the presence of the neighboring double bond.

By contrast, the prepared compounds are fairly stable toward acid agents. Heating of a methyl alcoholic solution of phenylethinylchloromethyl ketone with sodium sulfate solution in a sulfuric acid medium results in development of a characteristic reddish-brown color with an intense green fluorescence. This phenomenon is possibly associated with formation in the reaction mixture of a compound of the oxonium type due to cyclization of the formed chlorine-containing α-diketone. The cause of this phenomenon has not yet been closely studied.

EXPERIMENTAL

1. 1-Phenyl-4-chlorobutyne-1-one-3

To a solution of 30.6 g (0.3 mole) phenylacetylene and 100 ml absolute ether is added, with cooling, 7.9 g (0.3 mole) finely sliced sodium. At the conclusion of the energetic reaction, the mixture is refluxed for an hour until the metal has completely dissolved. The resultant suspension of sodium phenylacetylide is stirred, with cooling (ice-salt) in small portions into a solution of 35 g chloroacetyl chloride in 50 ml absolute ether in the course of an hour. After all has been added, the bath temperature is raised gradually to room temperature and the stirring continued for 4 hours. Addition is then made to the mixture of 150 ml cooled 5% hydrochloric acid, and the mixture is stirred for another 30 minutes. The ether layer is separated and the aqueous layer is extracted with ether; the combined extracts are washed with cold 1% sodium carbonate solution and dried over calcium chloride. The ester is distilled off and the residue fractionated in vacuum. The following fractions (at 7 mm) were collected: 1) to 40° 9.0 g; 2) 40-136° 1.5 g; 3) 136-138° 15.0 g; 4) residue 10.0 g.

The first fraction was unreacted phenylacetylene; it may be reused for synthesis. The third fraction rapidly crystallized almost completely. After recrystallization from ligroine it formed colorless needles with m.p. 37°. Yield 14.5 g.

Found %: C 66.85, 66.78; H 3.82, 3.78. $C_{10}H_7OCl$. Calculated %: C 67.22; H 3.90.

The substance is readily soluble in organic solvents, less soluble in ligroine, insoluble in water. It rapidly decolorizes a solution of permanganate in acetone and a solution of bromine in chloroform.

Dinitrophenylhydrazone. Prepared by the usual method in glacial acetic acid, from which it also recrystallizes in fine, golden needles with m.p. 170-171°.

Found %: N 15.82, 15.72. $C_{16}H_{11}O_4N_4Cl$. Calculated %: N 15.62.

Insoluble in water, benzene, ether; poorly soluble in alcohol; soluble in acetic acid.

II. 1-Phenyl-4-bromopentyne-1-one-3

This compound is prepared by a similar method from sodium phenylacetylide (from 15.32 g phenylacetylene, 3.9 g sodium in 70 ml absolute ether) and a solution of 36.6 g (0.17 mole) α-bromopropionyl bromide in 40 ml absolute ether. The following fractions were collected on distillation in vacuum: 1) to 40° 5 g (unreacted phenylacetylene); 2) 40-147° 1.5 g; 3) 147-152° 14.0 g; 4) residue 3.5 g.

A second distillation of the third fraction gave 11 g 1-phenyl-4-bromopentyne-1-one-3 with b.p. 145-146° at 6 mm. Amber-colored oil, slowly darkening when kept.

Found %: C 55.67, 55.59; H 3.79, 3.74. $C_{11}H_9OBr$. Calculated %: C 55.69; H 3.79.

The dinitrophenylhydrazone consists of fine yellow needles with m.p. 188.5-189°. Poorly soluble in alcohol, insoluble in water, soluble in acetic acid. Found %: N 13.29, 13.46. $C_{17}H_{13}O_4N_4Br$. Calculated %: N 13.45.

III. 1-Phenyl-4-bromohexyne-1-one-3

Prepared from 15.3 g (0.15 mole) phenylacetylene, 3.7 g sodium and 39.0 g (0.17 mole) α-bromobutyryl bromide. After vacuum-distillation of the reaction product, the following fractions were collected (at 8 mm): 1) to 40° 4.5 g (unreacted phenylacetylene); 2) 40-165° 1.5 g; 3) 165-177° 9.9 g; 4) residue 6.3 g.

A second distillation of the third fraction gave 9.7 g 1-phenyl-4-bromohexyne-1-one-3 with b.p. 167.5-168.5° at 7 mm. Amber-colored oil, slowly darkening when kept.

Found %: C 57.24, 57.33; H 4.45, 4.48. $C_{12}H_{11}OBr$. Calculated %: C 57.39; H 4.38.

Dinitrophenylhydrazone. Orange-yellow needles with m.p. 163-164°. Insoluble in water, poorly soluble in alcohol, soluble in acetic acid.

Found %: N 12.94, 12.79. $C_{18}H_{15}O_4N_4Br$. Calculated %: N 12.99.

IV. 1-Phenyl-4-bromo-4-methylpentyne-1-one-3

Prepared from 15.3 g (0.15 mole) phenylacetylene, 3.7 g sodium and 39.0 g (0.17 mole) α-bromoisobutyryl bromide. The following fractions were collected after vacuum-distillation (7 mm) of the reaction product: 1) to 40° 5.0 g (unreacted phenylacetylene); 2) 40-145° 4.0 g; 3) 145-150° 13.0 g; 4) residue 5.2 g.

A second distillation of the third fraction gave 8.8 g 1-phenyl-4-bromo-4-methylpentyne-1-one-3 with b.p. 146-148° at 7 mm. Amber oil, slowly darkening when kept.

Found %: C 57.28, 57.09; H 4.44, 4.28. $C_{12}H_{11}OBr$. Calculated %: C 57.39; H 4.38.

Dinitrophenylhydrazone. Orange-yellow needles with m.p. 173.5-174°. Insoluble in water, poorly soluble in alcohol, soluble in acetic acid.

Found %: N 13.08, 13.11. $C_{18}H_{15}O_4N_4Br$. Calculated %: N 12.99.

V. Reduction of 1-Phenyl-4-chlorobutyne-1-one-3 with Excess of Zinc Dust

To a solution of 7.5 g chloroketone in 150 ml alcohol was added 50 ml acetic acid followed, in small portions, by 13.5 g zinc dust, the temperature of the mixture being kept at about 40°. The reaction was completed by refluxing the mixture at 50°. The hot solution was then filtered from the excess of zinc dust, and the alcohol was distilled off. The residue formed two layers. It was extracted with ether and the extract washed with water and dried over sodium sulfate. On the following morning the crystals were filtered off from the extract (yield of crystals 0.5 g). After recrystallization from alcohol the product formed colorless needles with m.p. 160.5°. The ether was driven off the extract and the residue therefrom was distilled in vacuum to give the following fractions (at 13 mm): 1) to 110° a few drops; 2) 110-115° 2.0 g; 3) 115-150° a few drops; 4) 150-200° 1.5 g.

The fourth fraction crystallized completely in the receiver. The crystals were pressed and recrystallized from alcohol-ether mixture to give 0.9 g colorless crystals with m.p. 160° which did not depress the m.p. in admixture with the substance crystallizing from the extract. The mixed sample of both portions of the substance with 4,5-diphenyloctadione-2,7 [7] does not give a melting point depression.

The second fraction was converted by the usual method into the semicabazone which formed colorless crystals (from aqueous methyl alcohol) with m.p. 141-142°. A mixed sample with the semicarbazone of benzylacetone did not give a melting point depression.

VI. Reduction of 1-Phenyl-4-chlorobutyne-1-one-3 with a Molar Amount of Zinc Dust

Into a solution of 5.0 g chloroketone in 175 ml 7% methyl alcohol is introduced, portionwise (0.2 g portions over a period of an hour,) 2.3 g zinc dust, and addition is made simultaneously, in 2 ml portions, of 20 ml 25% acetic acid. Each portion of zinc dust was only introduced after the previous one had completely dissolved. The mixture was then shaken for another hour and then filtered, and the methyl alcohol driven off. The residue formed layers and was extracted with ether. The extracts were twice washed with water and dried over sodium sulfate. The ether was driven off and the residue distilled in vacuum, the following fractions being collected (at 5 mm): 1) to 110° a few drops; 2) 110-112° 2.1 g (52% of the theoretical); 3) 112-120° 0.4 g.

The second fraction had the following constants after a second vacuum distillation: b.p. 110-111° at 5 mm; n_D^{20} 1.5742; d_4^{20} 1.0257. (Literature data for phenylethinylmethyl ketone [4]: b.p. 122-124° at 13 mm; n_D^{20} 1.5728, d_4^{20} 1,024).

The dinitrophenylhydrazone formed orange-yellow crystals with m.p. 185-186°. A mixed test with the dinitrophenylhydrazone of phenylethinylmethyl ketone did not give a melting point depression.

Phenylmethylpyrazolone. Prepared by the method of Moureau and Brachin [8] and had m.p. 123-124° after recrystallization from 25% alcohol. A mixed test with an authentic specimen of phenylmethylpyrazolone did not give a melting point depression.

SUMMARY

1. Reaction of sodium phenylacetylide with acid chlorides of α-halo-substituted acids gives α-halo ketones of the acetylene series. Preparation was accomplished by this method, for the first time, of: 1-phenyl-4-chlorobutyne-1-one-3; 1-phenyl-4-bromopentyne-1-one-3; 1-phenyl-4-bromohexyne-1-one-3; and 1-phenyl-4-bromo-4-methylpentyne-1-one-3.

2. The structure of the prepared compounds was proved by reduction of the first member of the series, 1-phenyl-4-chlorobutyne-1-one-3, with zinc dust to phenylethinylmethyl ketone. When using excess of reducing agent, the reaction leads to benzylacetone and 4,5-diphenyloctadione-2,7.

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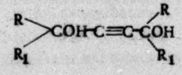
METHODS OF DETERMINATION OF THE STRUCTURE OF TERTIARY ACETYLENIC ALCOHOLS AND OF γ-ACETYLENIC GLYCOLS

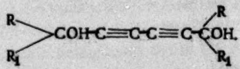
II. DETERMINATION OF THE STRUCTURE OF ACETYLENIC ALCOHOLS, γ-GLYCOLS AND DIACETYLENIC GLYCOLS BY OZONIZATION AND BY THE SPECTROGRAPHIC METHOD

A. I. Lebedeva, T. A. Mishnina and R. P. Ryskina

We know from previous investigations [1] that oxidation of acetylenic glycols with potassium permagnate in aqueous or acetone solution gives a ketone, an α-hydroxy acid and oxalic acid, i.e. the same products that must also be formed on oxidation of diacetylenic glycols with a conjugated system of triple bonds. Consequently this method cannot be used for determination of the structure of glycols having the general formula



and



We decided to apply ozonization and ultraviolet spectrographic analysis for the determination of the structure of these compounds.

Although the ozonization of acetylenic compounds was first given attention over 45 years ago, this field has still not been exhaustively investigated. There are still no unambiguous answers to the question of the structure of the ozonides of the acetylenic series, of the mechanism of the processes taking place during ozonization and during decomposition of the ozonides. Some investigators believe [2] that ozonization of the acetylenic bond proceeds through the stage of formation of 1,2-diketones which are then oxidized by hydrogen peroxide formed by decomposition of the ozonides, giving two saturated acids. Such diketones were isolated in the ozonization of diphenylacetylene and benzylphenylacetylene [3]. With the help of ultraviolet spectrography, Kahn and Newman [4] succeeded in showing that ozonization of stearolic acid gives 9,10-diketostearic acid.

We were unable to find in the literature any references to the ozonization of acetylenic γ-glycols and diacetylenic glycols. Before undertaking actual ozonizations, therefore, we found it necessary to select uniform conditions with respect to solvent, temperature, method of decomposition and analysis of the products of ozonolysis. In preliminary experiments it was established that the acetylenic compounds under investigation absorbed, at the most, 60-65% of the amount of ozone introduced. It was also established that methyl alcohol and ethylacetate react with ozone during ozonization in our conditions; we therefore chose chloroform as solvent. Ozonization was performed at −20°. when the ozonization temperature was lowered to −60°, the starting material came out of solution. Determinations were made throughout periods of 15 minutes of the amount of ozone entering the reaction vessel and leaving it. Ozonization was stopped after addition of the theoretically calculated amount of ozone. In Figure 1 (see also Table 3) on the ordinates is plotted the amount of ozone absorbed in unit time; the abscissas show the period of time. We see from the curves that the rate of ozonization of tetraethylbutynediol was constant up to the absorption of one molecule of ozone, and then fell rather sharply. In the ozonization of the diacetylenic compound, 3,8-dimethyl-4,6-decadiyne-3,8-diol, the rate was constant up to absorption of approximately one molecule of ozone, after which it gradually dropped until two molecules of ozone had been taken up. In this respect the rate of ozonization of the $-C\equiv C-C\equiv C-$ bonds is reminiscent of the rate of ozonization of conjugated dienic systems. Harries [5] had already established that in compounds containing two conjugated double bonds, the first molecule of ozone adds on much more rapidly than the second. We also know from a later investigation [6] that in the ozonization of compounds with two or three conjugated double bonds, only one molecule of ozone adds on quickly, and a gradual fall in the rate of ozone absorption is then observed.

During the ozonization of diethyldecadiynediol we observed that the solution changed color: in the first period the color became yellow; in the second period it changed from light-green to blue.

In the ozonization of tetra-p-tolylbutynediol and methyl-p-tolylethinyl carbinol, the speed is low and gradually decreases throughout the entire process. No inflection whatever could be observed in the curve after addition of one molecule of ozone. If we stopped the ozonization after addition of one molecule of ozone, we recovered up to 60% of the starting material unchanged. All this supported the view that in the case of aromatic constituents, ozone reacts not only with the triple bond but also with the aromatic nucleus. Results of analyses of the ozonolysis products appear in Table 2.

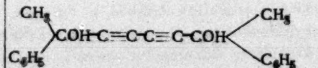
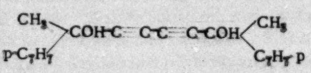
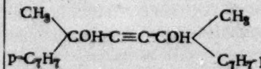
We see from this table that the structure of acetylenic γ-glycols of the aliphatic series can be determined by quantitative ozonization with arbitrary quantitative allowance for the ozonolysis products. This method, however, has a number of limitations. With increasing molecular weight of the substituents, the yield of oxalic acid increases while that of α-hydroxy acids decreases. The increase in oxalic acid yield is particularly large in ozonization of aliphatic-aromatic acetylenic glycols. Another drawback is the rather long period involved in the process of ozonization and in analysis of the ozonolysis products.

In the light of the above facts we decided to apply the spectrographic method to analysis of the diacetylenic compounds. We know that acetylenic compounds in which the triple bond is not conjugated with another unsaturated bond or with a carbonyl, nitro or nitroso group possess a strong absorption in the ultraviolet in the short-wave region not higher than 2200 A.

When the triple bond is conjugated, however, with one or several double or triple bonds, a considerable shift occurs in the maximum of light absorption toward the longer wave region and a significant increase in the intensity of absorption. Using the method of variable thickness of layer, we plotted on the SP-22 spectrograph the absorptions of the following compounds: 1) 3,8-dimethyl-4,6-decadiyne-3,8-diol; 2) 3,8-diethyl-4,6-decadiyne-3,8-diol; 3) 4,9-dimethyl-5,7-dodecadiyne-4,9-diol; 4) 2,9-dimethyl-3,8-diisopropyl-4,6-decadiyne-3,8-diol; and 5) 2,7-di-p-tolyl-3,5-octadiyne-2,7-diol. The plots showed that all of the investigated diacetylenic glycols have an absorption maximum in the 2400-2560 Å region. For quantitative characterization of the intensity of absorption, plots were constructed, with the SF-11 spectrophotometer (Beckmann system), of the absorption curves of the following compounds: 1) 2,5-di-p-tolyl-3-hexyne-2,5-diol; 2) 3,8-diethyl-4,6-decadiyne-3,8-diol; and 3) 2,7-di-p-tolyl-3,5-octadiyne-2,7-diol.

For comparison with our own results, Table 1 also contains data of other investigators. Some of these data were published when we had already completed the experimental part of the present investigation.

TABLE 1

No.	Formula	λ maximum (in A)	K	Literature
1	$\mathrm{(CH_3)_2COH{-}C{\equiv}C{-}C{\equiv}C{-}COH(CH_3)_2}$	2290 2410 2560	310 300 180	[7]
2	$\mathrm{(C_2H_5)COH{-}C{\equiv}C{-}C{\equiv}C{-}COH(C_2H_5)_2}$	2410 2560	317 201	Our data
3	 $\mathrm{(CH_3)(C_6H_5)COH{-}C{\equiv}C{-}C{\equiv}C{-}COH(CH_3)(C_6H_5)}$	2445 2580	1020 900	[8]
4	$\mathrm{(C_6H_5)_2COH{-}C{\equiv}C{-}C{\equiv}C{-}COH(C_6H_5)_2}$	2485 2610	2240 1660	[8]
5	 $\mathrm{(CH_3)(p{-}C_7H_7)COH{-}C{\equiv}C{-}C{\equiv}C{-}COH(CH_3)(C_7H_7{-}p)}$	2440 2580 2620 * 2720	1550 1170 1170 660	Our data
6	 $\mathrm{(CH_3)(p{-}C_7H_7)COH{-}C{\equiv}C{-}COH(CH_3)(C_7H_7{-}p)}$	2620 2720 *	388 328	Our data

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* The principal maximum of toluene is at 2620 Å.

It is seen from the data of Table 1 that diacetylenic glycols of the aliphatic series possess not less than two characteristic absorption maxima in the ultraviolet at 2410 and 2560 A.

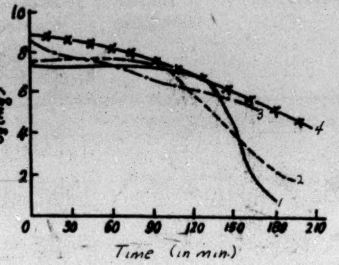

Fig. 1.

1) Tetraethylbutynediol; 2) dimethyldecadiynediol; 3) tetra-p-tolylbutynediol; 4) methyl-p-tolylethinyl carbinol.

The presence in the molecule of a diacetylenic glycol of aromatic substituents possessing their own specific absorption maxima has no appreciable influence on the position of the maxima characteristic of the $-C{\equiv}C-C{\equiv}C-$ bonds. This is demonstrable with particular clarity by the curves obtained when investigating acetylenic and diacetylenic compounds in the ultraviolet in the SF-11 spectrograph (Figs. 2 and 3).

Consequently the ultraviolet method permits the possibility of establishing the presence in the investigated product of a compound with a conjugated system of triple bonds.

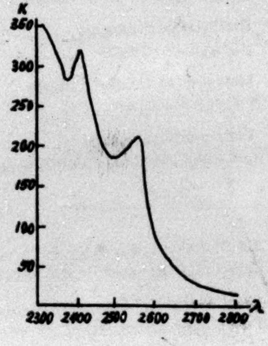

Fig. 2. Dimethyldecadiynediol.

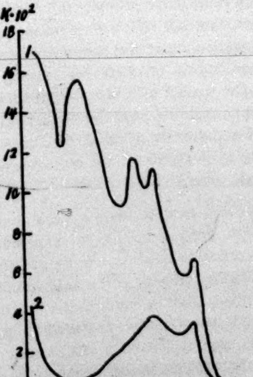

Fig. 3.

1) Di-p-tolyloctadiynediol; 2) symm.-dimethyldi-p-tolylbutynediol.

EXPERIMENTAL

Preparation of 4,9-dimethyl-5,7-dodecadiyne-4,9-diol. 20 g methyl-n-propylethinyl carbinol was added to a mixture consisting of 60 g ammonium chloride, 20 g cuprous chloride and 250 ml water. Oxygen was passed through the mixture with good stirring for 2 hours. The resultant precipitate was filtered off and the solution was extracted with ether. A total of 18.6 g solid product was obtained; this was repeatedly recrystallized from a mixture of benzene and ligroine (40-60°) and then from petroleum ether to form crystals in the form of small needles with m.p. 74-75°.

0.1038 g substance: 0.2877 g CO_2; 0.0937 g H_2O.
0.1886 g substance: 17.95 g benzene: Δt 0.230°.
0.0657 g substance: 15.4 ml CH_4 (14°, 773 mm).
Found %: C 75.61; H 10.10. M 222; act. H-atoms 2.18. $C_{14}H_{20}(OH)_2$. Calculated %: C 75.65; H 9.98. M 234; act. H-atoms 2.00.

From the residue after recrystallization could be separated crystals, melting at 100-104° (gradually), in very small quantity; these gave a melting point depression with the first isomer.

Preparation of 2,9-dimethyl-3,8-diisopropyl-4,6-decadiyne-3,8-diol. From 18 g diisopropylethinyl carbinol (technical), by the preceding method, was prepared 6.4 g of a solid product which after recrystallization from dilute alcohol came down in the form of lustrous scales with m.p. 118-119°.

The literature gives m.p. 115° [9].

TABLE 2

Preparation No.	Name of compound and formula	Physical constants	Quantity	
			Of compounds taken (in g)	Of ozone absorbed (in g) exper./theor.
1	Tetramethylbutynediol $(CH_3)_2COH-C\equiv C-COH(CH_3)_2$	M.p. 94-95°	4.0	3.36 1.35
2	Tetraethylbutynediol $(C_2H_5)_2COH-C\equiv C-COH(C_2H_5)_2$	M.p. 80-81°	4.0	1.02 0.97
3	Dimethyldiethylbutynediol $C_2H_5(CH_3)COH-C\equiv C-COH(CH_3)C_2H_5$	M.p. 52-53°	4.0	0.88 1.13
4	Diethylethinyl carbinol $(C_2H_5)_2COH-C\equiv CH$	B.p. 136-138°	4.9	2.00 1.71
5	Methyl-p-tolylethinyl carbinol $p\text{-}C_7H_7(CH_3)COH-C\equiv CH$	M.p. 34-35°	4.0	1.28 1.20
6	Tetra-p-tolylbutynediol $(p\text{-}C_7H_7)_2COH-C\equiv C-COH(C_7H_7\text{-}p)_2$	M.p. 154-155°	4.0	0.46 0.43
6a	Ditto	M.p. 154-155°	4.0	3.51 0.43
7	3,8-Dimethyl-4,6-decadiyne-3,8-diol $C_2H_5(CH_3)COH-C\equiv C-C\equiv C-COH(CH_3)C_2H_5$	M.p. 89-90°	2.0	0.98 0.98
8	4,9-Dimethyl-5,7-dodecadiyne-4,9-diol $n\text{-}C_3H_7(CH_3)COH-C\equiv C-C\equiv C-COH(CH_3)C_3H_7\text{-}n$	M.p. 74-75°	2.0	0.83 0.87

The remaining diacetylenic glycols were synthesized in the same manner.

Ozonization *. A weighed amount of the compound to be ozonized was dissolved in 40 ml chloroform and placed in a reaction vessel externally cooled with a mixture of ice and salt. An exception was represented by tetramethylbutynediol which we ozonized in solution in ethyl acetate because it was insoluble in chloroform. Through the reaction vessel was passed dry oxonized oxygen containing 4-6% ozone. The amount of ozone entering and leaving the reaction vessel during each 15 minute period was determined by titration with thiosulfate, while the amount of ozone absorbed was determined by difference. In the majority of experiments, ozonization was concluded after the theoretical amount of ozone had been absorbed, although in many experiments, the absorption of ozone continued with nearly the same velocity, as can be seen from the results enumerated in Table 3. The rate of ozonization is expressed in Table 3 in ml thiosulfate ($T_{Na_2S_2O_3} = 0.00221$ g/ml).

The prepared ozonides were worked up in the following manner: the solvent was filtered at the pump at room temperature, the ozonide was decomposed with water with heating until the oily drops had disappeared, and potassium carbonate was added to the solution until the reaction was alkaline. The volatile neutral products were distilled into an acetic acid solution of p-nitrophenylhydrazine, and the nonvolatiles were extracted with ether. For the purpose of extraction of the hydroxy acids, the acidified (with sulfuric acid) solution was extracted with ether in a separating funnel; for extraction of the oxalic acid, the solution was treated for 60-80 hours in a Soxhlet. The oxalic acid was determined as the calcium salt. The yield of oxalic acid (in %) was calculated in relation to the amount of prepared ozonide. In experiments 1 and 6a (Table 2), much more than the theoretically calculated amount of ozone was passed through. When the theoretical amount of ozone was passed through, much of the starting material was recovered unchanged.

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* Ozonization was carried out by the method of A. I. Yakubchik [10].

Table 2

Of ozonide obtained (in g) exper. theor.	Products of ozonolysis				
	Neutral (in g)	Hydroxy acids		Oxalic acid	
		Yield (in g)	M.p.	(g)	(%)
5.0 5.3	Acetone (traces)	$(CH_3)_2COH-COOH$ (4.1)	79-80*	None	None
4.9 5.0	Diethyl ketone (traces)	$(C_2H_5)_2COH-COOH$ (3.6)	77-78	0.002	0.11
5.6 5.1	None	$C_2H_5(CH_3)COH-COOH$ (2.3)	65-66	0.011	0.52
4.5 7.0	Diethyl ketone (traces)	$(C_2H_5)_2COH-COOH$ (2.4)	77-78	0.055	2.16
4.8 5.2	Methyl-p-tolyl ketone (1.77)	$p-CH_3C_6H_4COOH$ (1.8)	173	0.042	2.00
—	Tetra-p-tolylbutylnediol (2.50)	$(p-C_7H_7)_2COH-COOH$ (1.3)	131-132	None	None
4.5 4.4	Resin	$p-CH_3C_6H_4COOH$ (1.8)	176-177	0.092	11.35
2.7 3.0	Methylethyl ketone (0.10)	$C_2H_5(CH_3)COH-COOH$ (1.7)	65-66	0.300	30.0
2.5 2.9	Methyl-n-propyl ketone (0.1)	$n-C_3H_7(CH_3)COH-COOH$ (1.8)	50-51	0.250	30.6

TABLE 3

Preparation No.	Name of compound	Amount of ozone absorbed each 2 min. (in ml thiosulfate)
1	Tetramethylbutynediol	6.7; 6.6; 6.8; 6.4; 6.0; 6.1; 6.1; 1.2; 0.8
2	3,8-Dimethyl-4,6-decadiyne-3,8-diol	7.0; 6.9; 6.9; 6.9; 6.4; 6.0; 5.5; 4.4; 3.0; 2.4; 1.8.
3	Tetra-p-tolylbutynediol	10.6; 7.3; 7.1; 6.7; 6.6.
4	Methyl-p-tolylethinyl carbinol ...	8.0; 7.9; 7.7; 7.6; 7.1; 6.9; 6.4; 6.3; 6.2; 5.6; 5.1; 5.0; 4.5.

In experiment 1, the ozone apparently reacted with the solvent, while in experiments 6 and 6a it reacted with the aromatic nucleus of the substituents entering into the composition of the acetylenic compounds. In experiment 6 the ozonide was decomposed without distillation of the solvent because the ozonide was otherwise obtained in the form of a polymer which was not decomposed either by water or by an aqueous solution of potassium iodide.

After distillation of the ether, the hydroxy acids were recrystallized from benzene. In experiment 6a, p-toluic acid separated instead of di-p-tolylglycolic acid.

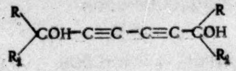
Spectroscopic analysis of the compounds was carried out in ethyl alcohol solution; an 0.5% solution was taken with the SP-22 spectrograph; a solution of 0.03-0.01 moles per liter was taken with the SF-11.

SUMMARY

1. The structure of acetylenic γ-glycols of the aliphatic series can be determined by quantitative ozonization followed by quantitative analysis of the products of ozonolysis. The rate of ozonization of these glycols is constant up to absorption of the theoretical amount of ozone, after which it falls fairly sharply.

2. The rate of ozonization of aliphatic-aromatic acetylenic alcohols and γ-glycols falls slowly throughout the whole process of ozonization; no inflection whatever is observed in the curve after addition of one molecule of ozone. A fairly large amount of oxalic acid (2-10%) is found among the products of ozonolysis, so that this method is little suited to the determination of the structure of these compounds.

3. The structure of diacetylenic glycols of the type of



where R and R_1 are aliphatic substituents may be determined by quantitative ozonization. The rate of ozonization of these glycols is constant up to absorption of one molecule of ozone, after which it gradually begins to drop.

4. Diacetylenic glycols with the above structure possess two characteristic maxima in the ultraviolet at 2140 A and 2560 A. The position of the maxima does not change appreciably when R and R_1 are aromatic radicals, but other maxima appear which correspond to the aryl substituents. The ultraviolet method is applicable to the analysis of diacetylenic glycols containing a conjugated system of triple bonds.

5. The diacetylenic glycol 4,9-dimethyl-5,7-dodecadiyne-4,9-diol has been synthesized for the first time, and it has been shown that the maxima of the absorption spectra of this compound in the ultraviolet are in the region of 2400 and 2600 A.

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*See Consultants Bureau English Translation, p. 593 ff.

THE PROBLEM OF THE FORMATION OF ORGANOMETALLIC COMPOUNDS BY REACTION OF AROMATIC SILANES WITH METALLIC CHLORIDES

I. FORMATION OF ORGANOALUMINUM COMPOUNDS BY REACTION OF PHENYLCHLOROSILANES WITH $AlCl_3$

A. Ya. Yakubovich and G. V. Motsarev

The reaction of aromatic silanes with $AlCl_3$ has been studied with reference to compounds such as diphenyldichlorosilane [1], tetraphenylsilane [2] and triethylphenylsilane [3]. In these cases $AlCl_3$ proved to be an extremely active dearylating agent which brought about cleavage of the organosilicon molecules at the Si — C bond. It was established that this cleavage is effected with great ease even in ordinary conditions and is accompanied by formation of aromatic organoaluminum compounds. This was proved by transformation of the latter into benzene by the action of water.

These data actually comprise all that is known about the action of $AlCl_3$ on aromatic organosilicon compounds. There are no data at all for the influence of the ratio of components (silane and $AlCl_3$) or for the effect of substituents in the aromatic nucleus on the course and on the results of reaction between aromatic silanes and $AlCl_3$. Moreover, the formation of benzene by treatment of the products with water constitutes the sole evidence that organoaluminum compounds are formed and cannot be regarded as conclusive evidence.

For these reasons we undertook an investigation of these reactions, starting from phenyltrichlorosilane, diphenyldichlorosilane and their derivatives.

We first studied the unsubstituted phenyltrichlorosilane. It was found that this compound, just like the other silanes, reacts with freshly sublimed $AlCl_3$ with cleavage at the Si—C bond even at a temperature of 30-35°. The product of this reaction, apart from $SiCl_4$ (isolated in a yield of 50% of the theoretical), is actually phenylaluminum dichloride, as could be inferred not only from the formation of benzene by treatment with water (after distilling off the $SiCl_4$) but also from the ease of substitution of the $AlCl_2$ residue by the CH_3CO- or PCl_2- group when reacted with CH_3COCl or PCl_3.

$$C_6H_5SiCl_3 + AlCl_3 \longrightarrow C_6H_5AlCl_2 + SiCl_4; \qquad (1)$$

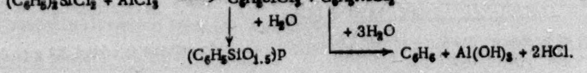
$$C_6H_5AlCl_2 + 3H_2O \longrightarrow C_6H_6 + Al(OH)_3 + 2HCl; \qquad (2)$$

$$C_6H_5AlCl_2 + CH_3COCl \longrightarrow C_6H_5COCH_3 + AlCl_3; \qquad (3)$$

$$C_6H_5AlCl_2 + PCl_3 \longrightarrow C_6H_5PCl_2 + AlCl_3. \qquad (4)$$

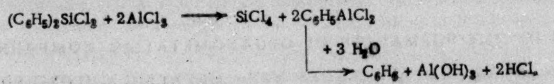
Yields of benzene, acetophenone and $C_6H_5PCl_2$ in reactions (2), (3) and (4) were respectively 55.5, 75.0 and 83.4%.

Diphenyldichlorosilane also reacts with $AlCl_3$ at the ordinary temperature, but the reaction course depends on the molar ration of components. Thus with a molar ration of diphenyldichlorosilane to $AlCl_3$ of 1:1 at 30-35°, the reaction products (after decomposition of the reaction mass with water) were benzene (isolated in amount corresponding to a yield of 38% of the theoretical) and a resin (formed by hydrolysis of the phenyltrichlorosilane formed on cleavage) in yield of 65% of the theoretical:



$$\begin{tikzcd}
(C_6H_5)_2SiCl_2 + AlCl_3 \arrow[r] & C_6H_5SiCl_3 \arrow[d, "+ H_2O"] + & C_6H_5AlCl_2 \arrow[d, "+ 3H_2O"] & \\
 & (C_6H_5SiO_{1.5})p & \arrow[r] & C_6H_6 + Al(OH)_3 + 2HCl.
\end{tikzcd}$$

With a molar ratio of reactants of 1:2 at 30°, there are formed silicon tetrachloride (yield 60%) and benzene (yield 61.2%), the latter due to decomposition by water of the residue after distilling off the silicon tetrachloride.



$$\begin{tikzcd}(C_6H_5)_2SiCl_2 + 2AlCl_3 \arrow[r] & SiCl_4 + 2C_6H_5AlCl_2 \arrow[d, "+3H_2O"] \\ & C_6H_6 + Al(OH)_3 + 2HCl\end{tikzcd} \qquad (6)$$

Derivatives of phenylchlorosilanes containing nuclear substituents that were selected for this investigation were p-chloro- and p-bromophenyltrichlorosilanes, as well as (p-chlorophenyl)-phenyldichlorosilane, all prepared with the help of the Grignard synthesis [4].

Halogen-substituted phenylchlorosilanes behave with $AlCl_3$ like unsubstituted phenyl derivatives of silane.

These cleavage reactions undoubtedly lead to formation of organoaluminum compounds containing halogen atoms in the phenyl ring:

$$C_6H_4XSiCl_3 + AlCl_3 \longrightarrow C_6H_4XAlCl_2 + SiCl_4, \qquad (7)$$

where X= Cl, Br, etc.

This follows both from the formation of the corresponding halobenzenes by the action of water on the cleavage products and from their reactions with acetyl chloride and phosphorus trichloride which were studied for p-chloro- and p-bromo- phenyltrichlorosilanes:

$$p\text{-}C_6H_4Cl(Br)SiCl_3 + AlCl_3 \longrightarrow p\text{-}C_6H_4Cl(Br)AlCl_2 + SiCl_4; \qquad (8)$$

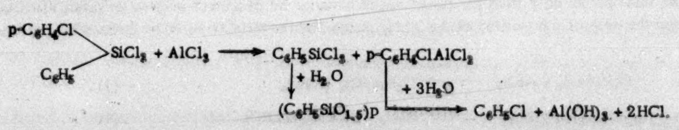
$$p\text{-}C_6H_4Cl(Br)AlCl_2 + CH_3COCl \longrightarrow p\text{-}C_6H_4Cl(Br)COCH_3 + AlCl_3; \qquad (9)$$

$$p\text{-}C_6H_4Cl(Br)AlCl_2 + PCl_3 \longrightarrow p\text{-}C_6H_4Cl(Br)PCl_2 + AlCl_3. \qquad (10)$$

The yields of $p\text{-}C_6H_4ClCOCH_3$, $p\text{-}C_6H_4ClPCl_2$ and $p\text{-}C_6H_4BrPCl_2$ in reactions (8), (9) and (10) were respectively 53, 77.4 and 72.6%.

(p-Chlorophenyl)-phenyldichlorosilane reacts with $AlCl_3$ in a similar manner to diphenyldichlorosilane; in this case we may have either complete or partial cleavage of the molecule, depending on molar ratios of reactants.

On mixing $(p\text{-}C_6H_4Cl)\,C_6H_5SiCl_2$ with $AlCl_3$ in 1:1 molar ratio, cleavage takes place in the first instance of that radical which contains the substituent, as indicated by the isolation from the reaction products (after decomposition of the reaction mass with water) of chlorobenzene and resin (the latter formed by hydrolysis of the $C_6H_5SiCl_3$ resulting from the cleavage).



$$\begin{tikzcd}(p\text{-}C_6H_4Cl)(C_6H_5)SiCl_2 + AlCl_3 \arrow[r] & C_6H_5SiCl_3 \arrow[d, "+H_2O"] + p\text{-}C_6H_4ClAlCl_2 \arrow[rd, "+3H_2O"] & \\ & (C_6H_5SiO_{1.5})p & C_6H_5Cl + Al(OH)_3 + 2HCl\end{tikzcd} \qquad (11)$$

Consequently the introduction of halogen atoms into the aromatic nucleus of a chlorosilane intensifies the reactivity of the Si—C bond toward $AlCl_3$.

It should be noted that the above-described readily proceeding reactions with $AlCl_3$ of phenylchlorosilanes and their derivatives containing a substituent in the aromatic nucleus show that the replacement of SiX_3 groups by $AlCl_2$ residues may evidently be utilized as a method of synthesis of organoaluminum compounds of the aromatic series containing various substituents in the nucleus. The field of investigation is an interesting one when we consider that the possibilities of preparation of this type of organosilicon compound are rather wide, and that the transformations of the organoaluminum compounds are very diverse and proceed easily.

EXPERIMENTAL

Reaction of Phenyltrichlorosilane with $AlCl_3$

a) Preparation of benzene. To 5.0 g (0.023 mole) phenyltrichlorosilane is added 3.1 g (0.023 mole) freshly sublimed aluminum chloride. Addition of the latter is accompanied by slight heating of the mixture which acquires a red color. The mixture is left for 48 hours at 25-35°. The liquid mass is carefully distilled in vacuum from the reaction flask on a water bath through a condenser. In the receiver, cooled with acetone-carbon dioxide mixture (−60°), was collected a liquid with b.p. 55-57° and a pungent odor. The b.p. and density (d_4^{20} 1.4840) were identical with those of silicon tetrachloride. Yield 2.0 g or 50% of the theoretical.

The brown, semisolid residue in the reaction flask was carefully (at − 50°) decomposed with water and distilled with steam. The layer of liquid on the surface of the aqueous distillate was extracted with ether and dried over calcium chloride. After removing the ether, the residue was distilled on the water bath to give a liquid with b.p. 79-81°, identical in respect to b.p. and density (d_4^{20} 0.879) with benzene. Yield 1.0 g or 55.5% of the theoretical. For further identification the benzene was converted with nitration mixture into a crystalline substance which melted at 89.5° after recrystallization from alcohol and drying. The m.p. is that of m-dinitrobenzene. Yield 81% of the theoretical, calculated on the benzene.

b) Preparation of acetophenone. To 5.0 g (0.023 mole) phenyltrichlorosilane was added 3.1 g (0.023 mole) freshly sublimed aluminum chloride. To the residue remaining after distillation of the silicon tetrachloride (see preceding experiment) was added 2.0 g acetyl chloride in the cold. The mixture was thereupon heated for ½ hour at 50-80°, after which it was carefully treated with iced water while cooling (−30°). The separated oil was extracted with ether and the ethereal solution was washed with water and dried over calcium chloride. The ether was distilled off and the oily residue partly crystallized on standing. The crystals were separated by freezing the oil at 0°. M.p. 20.2° (from alcohol). A mixed test of these crystals with synthetic acetophenone did not give a melting point depression. The prepared acetophenone was also identified through the semicarbazone whose m.p. of 198-199° agreed with that of acetophenone semicabazone (198-200°).

Yield of acetophenone 2.1 g or 75% of the theoretical calculated on phenyltrichlorosilane. Yield of semicarbzone 81% of the theoretical, calculated on the acetophenone.

c) Preparation of phenyldichlorophosphine. 20.0 g (0.094 mole) phenyltrichlorosilane and 13.9 g (0.104 mole) anhydrous, freshly sublimed aluminum chloride were put into a round-bottomed flask connected to a reflux condenser and a receiver cooled with acetone-carbon dioxide mixture (−40°), and fitted with a calcium chloride tube. When the reactants were stirred, the mass turned red. The reaction was speeded up by heating for 10 hours at 70-80° with simultaneous removal of the silicon tetrachloride formed (the whole system was connected to a vacuum). In the receiver was collected 13.9 g $SiCl_4$ or 87% of the theoretical.

To the brown, semisolid residue remaining after removal of the $SiCl_4$ was added stepwise 13.0 g (0.094 mole) phosphorous trichloride. After the addition the mixture became liquid. It was heated for an hour at 80-90°, and then addition was made (gradually) of 17.2 g (0.112 mole) phosphorous oxychloride (as a complexing agent for removal of $AlCl_3$), which led to formation of a granular precipitate.

The precipitate was treated with several portions of petroleum ether, the extracts were combined, the petroleum ether distilled off and the residue distilled in vacuum to give 12.8 g (76% of the theoretical) phenyldichlorosilane in the form of a highly refractive, light-yellow liquid with b.p. 140-141° at 57 mm, fuming in the air and possessing a sharp, unpleasant odor.

Reaction of Diphenyldichlorosilane with $AlCl_3$

a) Preparation of benzene and phenyltrichlorosilane. A mixture (prepared with cooling) of 7.0 g (0.027 mole) diphenyldichlorosilane and 4.1 g (0.03 mole) freshly sublimed aluminum chloride was stood for 4 hours at 30-35°. The mass acquired a dark-red color. The cooled (to−30°) mass was treated with water (acidified with sulfuric acid) and distilled with steam. The benzene layer on the surface of the aqueous distillate wasextracted with ether and dried over calcium chloride. After distilling off the ether, the residue (benzene) was distilled on the water bath to give 0.8 g liquid with b.p. 78-80° and d_4^{20} 0.880. Yield of benzene 38.0% of the theoretical calculated on the diphenyldichlorosilane.

The residue in the distillation flask (2.2 g), after steam distillation, consisted of a light-yellow, transparent resin whose analysis for silicon corresponded to that of the resin prepared from phenyltrichlorosilane. Silicon found: 21.3%; required: 21.7%.

The yield of phenyltrichlorosilane, based on the amount of separated resin, was 65% of the theoretical calculated on the amount of diphenyldichlorosilane taken for the reaction.

b) Preparation of benzene and $SiCl_4$. To 8.0 g (0.032 mole) diphenyldichlorosilane was added (with cooling) 8.5 g (0.064 mole) aluminum chloride. The mixture was stood for 72 hours at 30-35°. The reaction mass had a dark-red color.

The liquid mass was carefully distilled in vacuum on a water bath. In the receiver, cooled with acetone-carbon dioxide mixture (−60°) collected a liquid with b.p. 56-57° and a pungent odor, resembling in boiling pt. and density (d_4^{20} 1.4841) silicon tetrachloride. Yield 3.3 g or 60% of the theoretical.

The semisolid brown residue after distillation of the $SiCl_4$ was decomposed with cold water. Appropriate treatment (see above) gave a liquid with a b.p. 79-80° whose density (d_4^{20} 0.876) also identified it as benzene. Yield 3 g or 61.2% of the theoretical.

Reaction of p-Chlorophenyltrichlorosilane* with $AlCl_3$.

a) Preparation of chlorobenzene. To 5.0 g (0.02 mole) p-chlorophenyltrichlorosilane was added 2.67 g (0.02 mole) aluminum chloride. The mixture turned red when stirred. It was left for 48 hours at room temperature and then carefully decomposed with water while cooling (−50°). Working-up as before (see preceding experiments) gave a liquid with b.p. 130-132°. The b.p. and density (d_4^{20} 1.1071) agreed with those of chlorobenzene. Yield 1.3 g or 56.5% of the theoretical. For further identification the prepared chlorobenzene was converted with nitrating mixture into a crystalline substance with m.p. 82.6° after recrystallization from alcohol and drying. This is the m.p. of p-chloronitrobenzene. Yield 75% of the theoretical, calculated on the chlorobenzene.

b) Preparation of p-chloroacetophenone. To 2.8 g (0.011 mole). p-chlorophenyltrichlorosilane was added 1.5 g (0.011 mole) aluminum chloride. The mixture stood for 24 hours at room temperature, after which 0.9 g acetyl chloride was added in the cold. After the mixture had been heated at 70-80° for 20 minutes, it was carefully decomposed (cooling at −30°) with iced water. The resultant oil partly crystallized on standing. After suitable treatment (see above details for acetophenone) crystals were obtained which, after recrystallization from alcohol had m.p. 19.6° (p-chloroacetophenone melts at 20°). Found chlorine 22.7%; required 22.9%. Yield 0.9 g or 53% of the theoretical. The prepared p-chloroacetophenone was identified as the oxime whose m.p. of 96° corresponded to that of p-chloroacetophenone oxime (95°). Yield of oxime 60% of the theoretical.

c) Preparation of p-chlorophenyldichlorophosphine. 10.0 g (0.04 mole) p-chlorophenyltrichlorosilane was stirred with 6.0 g (0.045 mole) freshly sublimed aluminum chloride and 5.7 g (0.041 mole) phosphorus trichloride. The mixture was heated for 2 hours on a water bath at 80°, after which the $SiCl_4$ was distilled off (6.3 g or 90.7% of the theoretical), and to the residue was gradually added 7.0 g (0.045 mole) phosphorus oxychloride. Isolation of p-$C_6H_4ClPCl_2$ was effected on the same lines as for $C_6H_5PCl_2$ (see above). There was obtained 6.6 g p-chlorophenyldichlorophosphine in the form of a colorless, oily liquid with an unpleasant odor; b.p. 252-253°; d_4^{20} 1.4203. Yield 77.4% of the theoretical, calculated on the p-chlorophenyltrichlorosilane.

Reaction of p-Bromophenyltrichlorosilane with $AlCl_3$.

Preparation of p-bromophenyldichlorophosphine. 10.0 g (0.034 mole) p-bromophenyltrichlorosilane** was stirred with 5.0 g (0.037 mole) aluminum chloride and 4.7 g (0.034 mole) phosphorus trichloride. The mixture was heated for 2 hours on a water bath at 80°, following which the $SiCl_4$ was distilled off (5.2 g or 89.6% of the theoretical), and to the residue was gradually added 5.9 g (0.038 mole) phosphorus oxychloride. The p-$C_6H_4BrPCl_2$ was isolated by the same procedure as before (see preceding experiment). There was obtained 6.4 g p-bromophenyldichlorophosphine in the form of a colorless, strongly refractive, viscous liquid with b.p. 270°, d_4^{20} 1.6861. Yield 72.6% of the theoretical calculated on p-bromophenyltrichlorosilane taken in the reaction.

Reaction of (p-Chlorophenyl)-phenyldichlorosilane with $AlCl_3$.

A mixture of 5.0 g (0.017 mole) (p-chlorophenyl)-phenyldichlorosilane *** and 2.5 g (0.019 mole) freshly sublimed $AlCl_3$ was stood for 5 hours at 30-35°, following which it was treated under cooling (−30°) with water acidified with sulfuric acid, and distilled with steam. Working-up as in the preceding experiments gave a liquid with b.p. 131-132° identical in b.p. and density (d_4^{20} 1.1074) with chlorobenzene. Yield 1.0 g or 50% of the theoretical.

The residue in the flask (1.3 g) was steam distilled to give a yellow resin whose analysis for silicon corresponded to that of the resin prepared from phenyltrichlorosilane. Silicon found: 21.2%; required 21.7%.

The yield of phenyltrichlorosilane as resin was 57% of the theoretical, calculated on the (p-chlorophenyl)-phenyldichlorosilane taken in the reaction.

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* Prepared by reaction of p-chlorophenyl magnesium bromide with $SiCl_4$.

** Prepared by reacting p-bromophenyl magnesium bromide with $SiCl_4$.

*** Prepared from p-chlorophenyl magnesium bromide and phenyltrichlorosilane.

SUMMARY

1. A study was made of the reaction of $AlCl_3$ with phenyltrichlorosilane, diphenyldichlorosilane and their derivatives: p-chloro- and p-bromophenyltrichlorosilanes and (p-chlorophenyl)-phenyldichlorosilane. The effects of ratios of reactants (chlorosilane and $AlCl_3$) and of the presence of substituents in the aromatic nucleus on the course and results of these reactions were investigated.

2. It was shown from the transformations of the products of reaction of arylchlorosilanes with $AlCl_3$ that the intermediate products in these reactions are the corresponding organoaluminum compounds.

3. The action of acetyl chloride and PCl_3 on the intermediately formed organoaluminum compounds gives good yields of arylalkyl ketones and aryldichlorophosphines containing substituents such as chlorine and bromine in the nucleus.

4. The possibility is noted of using the reactions of arylchlorosilanes and their derivatives with $AlCl_3$ for syntheses of various organoelement compounds on the same lines as the described syntheses of phosphines.

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SYNTHESIS AND PROPERTIES OF SOME α-NAPHTHYL-AMINO- AND α-NAPHTHYLAMINOPHENYLSILANES

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In our previous investigations [1,2] were reported organomagnesium and -lithium syntheses of various organosilicon compounds containing α-naphthyl radicals. We thus prepared for the first time the following types of organosilicon compounds: $ArSiR_3$, Ar_2SiR_2 and Ar_3SiR, where $Ar=\alpha\text{-}C_{10}H_7$, and $R=OC_2H_5$, $n.\text{-}C_4H_9$ and C_6H_5.

Those investigations had established that reaction of α-naphthyl magnesium bromide with tetraethoxysilane only results in addition of two α-naphthyl radicals to the silicon atom, due to presence of considerable steric hindrances inherent in the α-naphthyl radical. When magnesium is replaced by lithium, the addition only proceeds up to the formation of tri-α-naphthylethoxysilane. For the above reason, tetra-α-naphthylsilane is not formed even when silicon tetrachloride is boiled in ether with excess of α-naphthyllithium. In these conditions the reaction comes to an end with formation of only tri-α-naphthylchlorosilane [3]. It is interesting to note that the α-naphthyl radical containing a substituent in the second benzene ring, say in the para-position, in similar synthesis conditions forms tetra-α-naphthylsilane in very good yield (81%) [4]. It was also established that α-naphthyl-n-butysilane and di-α-naphthyldi-n-butylsilane are obtained in up to 60% yields via the organolithium and -magnesium compounds, whereas tri-α-naphthyl-n-butylsilane was obtained in only 22% yield when starting from tri-α-naphthylchlorosilane and n-butyllithium [3].

Concerning the synthesis of α-naphthyltriphenylsilane, it must be noted that we prepared it by reacting α-naphthyltriethoxysilane with excess of phenyl magnesium bromide, whereas its corresponding hydrocarbon – α-naphthyltriphenylmethane could not be prepared by the organomagnesium synthesis; as we know, in these conditions the α-naphthyldiphenylmethyl free radical is formed [5]. Di-α-naphthyldiphenyl- and tri-α-naphthylphenylsilanes were obtained in lower yields (60 to 27%) with the help of organolithium compounds.

In the present investigation, starting from the corresponding α-naphthylfluorosilanes, the aim was to prepare α-naphthylamino- and α-naphthylaminophenylsilanes and to clarify their physicochemical properties. The composition and properties of the starting materials as well as of the compounds now synthesized by us for the first time are set forth in the table.

Physicochemical Properties, Reaction Components and Yields of α-Naphthylfluoro-, amino- and -aminophenylsilanes.

Name of Substance	M.p.	Reaction Components	Yields (%)	Literature References
α-Naphthytrifluorosilane	Liquid	$C_{10}H_7MgBr + SiF_4$	–	[6]
Di-α-naphthyldifluorosilane	79-81°	$C_{10}H_7MgBr + SiF_4$	22	[6]
Tri-α-Naphthylfluorosilane	226-227	$C_{10}H_7MgBr + SiF_4$	26	[7]
α-Naphthylaminosilane	–	$C_{10}H_7SiF_3 + NH_3$	–	Unstable
Di-α-naphthyldiaminosilane	154-156	$(C_{10}H_7)_2SiF_2 + NH_3$	Quantitative	Prepared by us
Tri-α-naphthylaminosilane	204-206	$(C_{10}H_7)_3SiF + NH_2Na$	50	Prepared by us
α-Naphthyltriaminophenysilane	176-179	$C_{10}H_7SiF_3 + C_6H_5NH_2$	Quantitative	Prepared by us
Di-α-naphthyldiaminophenylsilane	184-186	$(C_{10}H_7)SiF_2 + C_6H_5NH_2$	72	Prepared by us
Tri-α-naphthylaminophenylsilane	198-200	$(C_{10}H_7)_3SiF + C_6H_5NHNa$	27	Prepared by us

The starting α-naphthylfluorosilanes listed in the table were prepared by passing into an ethereal solution of α-naphthyl magnesium bromide a stream of silicon fluoride prepared from sodium fluosilicate and concentrated sulfuric acid in presence of finely pulverized glass powder; depending on the molar ratios of silicon fluoride to α-bromo-naphthyl magnesium and on the reaction temperature, there is formed either α-naphthyltrifluorosilane in admixture with di-α-naphthyldifluorosilane or only tri-α-naphthylfluorosilane.

In α-naphthylfluorosilanes, depending on the number of sterically hindering α-naphthyl radicals attached to the silicon atom, the replacement of fluorine by hydroxyl, amino or aminophenyl groups proceeds at varying velocities. Thus, whereas in α-naphthyltrifluorosilane the fluorine is quickly hydrolyzed by acidified water even in the cold, in di-α-naphthyldifluorosilane the fluorine is quite stable even in 50% acetic acid.

The fluorine is particularly firmly combined in tri-α-naphthylfluorosilane in which it is hydrolyzed with difficulty by hot 20-25% NaOH solution.

These factors lead to α-naphthylfluorosilanes in question reacting at different rates with ammonia gas and aniline. When ammonia, for example, is passed into an ethereal solution of α-naphthyltrifluorosilane, heat is developed and a flocculent precipitate is formed, evidently a mixture of α-naphthylaminosilanes which are easily hydrolyzed by moist air to form resinous polymers. But the replacement of fluorine in di-α-naphthyldifluorosilane by the amino group takes place even on heating the ethereal solution with formation of di-α-naphthylaminosilane, which is quite stable to moisture. This compound melts at 154-156° and solidifies to a vitreous mass. In tri-α-naphthylfluorosilane, the fluorine is replaced with difficulty only after prolonged boiling in toluene with excess of sodamide. The resultant tri-α-naphthyaminosilane is an amorphous substance melting at 202-204°. The only analog reported in the literature, triphenylaminosilane, melts at 55-56° [8].

Concerning α-naphthylaminophenylsilanes, here also α-naphthyltriaminophenylsilane is formed more easily; by heating of α-naphthyltrifluorosilane in toluene to 60-70° with excess of aniline, it is formed in quantitative yield. On the other hand, the formation of di-α-naphthyldiaminophenylsilane requires prolonged boiling. Tri-α-naphthylaminophenylsilane is formed in 27% yield only after boiling tri α naphthylfluorosilane for 6 hours in toluene with excess of sodium anilide.

EXPERIMENTAL

The starting substances were α-naphthyltrifluoro di-α-naphthyldifluoro- and tri-α-naphthylfluorosilanes, prepared [6,7] by passing the appropriate amounts of $SiCl_4$ into an ethereal solution of α-naphthyl magnesium bromide.

α-Naphthyltriaminosilane $\alpha\text{-}C_{10}H_7Si(NH_2)_3$. Dry ammonia was passed for 30 minutes into a solution of 6.0 g α-naphthyltrifluorosilane in 50 ml absolute ether. Heat was developed and an abundant amorphous precipitate came down. In contact with moist air it rapidly hydrolyzes with evolution of ammonia and formation of a resin (soluble in organic solvents) which burns with a smoky flame and leaves a residue of silica.

Di-α-naphthyldiaminosilane $(\alpha\text{-}C_{10}H_7)_2Si(NH_2)_2$. A stream of dry ammonia was passed into a solution heated to 30-33° of 8.0 g di-α-naphthyldifluorosilane in 50 ml ether for 1 hour. The precipitate was filtered off and twice recrystallized from pyridine. Yield 7.6 g di-α-naphthyldiaminosilane in the form of a fine, colorless powder, melting at 154-156° and solidifying to a vitreous mass with a light-yellow color.

Found % Si 8.6, 8.4; N 8.6. $C_{20}H_{18}SiN_2$. Calculated % Si 8.9; N 8.9.

Tri-α-naphthylaminosilane $(\alpha\text{-}C_{10}H_7)_3SiNH_2$. To 8.5 g tri-α-naphthylfluorosilane dissoved in 50 ml toluene was added 6.0 g freshly prepared sodamide [9]. With precautions against entry of moisture from the air, the solution was boiled for 6 hours; the flocculent precipitate of sodium fluoride was filtered off. Three crystallizations from toluene gave 4.2 g tri-α-naphthylaminosilane as a fine colorless powder, melting at 204-206° and about 3 g unreacted tri-α-naphthylfluorosilane.

Found %: Si 6.1, 6.0; N 3.2, 3.1. $C_{30}H_{23}SiN$. Calculated %: Si 6.5; N 3.2.

α-Naphthyltriaminophenylsilane $\alpha\text{-}C_{10}H_7Si(NHC_6H_5)_3$. To 6.5 g α-naphthyltrifluorosilane dissolved in 50 ml toluene was added 9.5 g freshly distilled aniline, and the solution was heated for an hour at 60-70°. After removal of the aniline hydrofluoride, the product was recrystallized from toluene to give 12.2 g α-naphthyltriaminophenylsilane, melting at 176-178° and solidifying to a vitreous mass.

Found %: Si 6.2, 5.9; N 11.5, 11.6. $C_{28}H_{25}SiN_3$ Calculated %: Si 6.5; N 11.2.

Di-α-naphthyldiaminophenylsilane $(\alpha\text{-}C_{10}H_7)_2Si(NHC_6H_5)_2$. 6.5 g di-α-naphthyldifluorosilane and 8 g freshly distilled aniline were boiled in 50 ml toluene for 5 hours. Removal of the toluene-insoluble precipitate was followed by separation of 6.7 g fine powder of di-α-naphthyldiaminophenylsilane, melting at 184-186° and solidifying to a vitreous mass.

Found %: Si 6.3, 5.8; N. 6.2, 6.4. $C_{34}H_{26}SiN_2$. Calculated %: Si 6.0; N 6.0.

Tri-α-naphthylaminophenylsilane $(\alpha\text{-}C_{10}H_7)_3SiNHC_6H_5$. To a freshly prepared solution of sodium anilide prepared by boiling 8 g aniline for 4 hours with excess sodium in 50 ml toluene, was added 8.5 g tri-α-naphthylfluorosilane, and the solution was again boiled for 6 hours. Removal of the sodium fluoride was followed by isolation from the solution of 2.7 g tri-α-naphthylaminophenylsilane, melting at 198-200°, and about 4 g of unreacted tri-α-naphthylfluorosilane.

Found %: Si 5.3, 5.1; N 2.8, 2.5. $C_{36}H_{27}SiN$. Calculated %: Si 5.6; N 2.8.

SUMMARY

1. The fluorine in α-naphthyltrifluoro- and di-α-naphthyldifluorosilanes can be readily replaced by the amino or aminophenyl group by the action of ammonia or aniline.

2. The fluorine of tri-α-naphthylfluorosilane can only be replaced by boiling the compound in toluene with excess of sodamide or sodium anilide.

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STERIC HINDRANCES IN ORGANOMAGNESIUM REACTIONS

XVI. PREPARATION OF KETONES BY REACTION OF ACID CHLORIDES WITH ORGANOMAGNESIUM COMPOUNDS

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Continuing the study of the method for preparing ketones based on reaction of acid chlorides with organomagnesium compounds [1,2], we set out to establish the possibility of synthesizing alkoxyl-containing ketones by this method.

As we know, the application of the Gustavson-Friedel-Crafts method to the preparation of such ketones is not always successful due to the cleaving action of aluminum chloride on alkoxyl groups.

Although Fuson and his co-workers [3,4,5] showed that the Grignard reagent sometimes reacts with methoxybenzonitrile with substitution of the methoxyl gruup by the radicals of the organomagnesium compounds, this substitution was not observed in a single case in the experimental conditions of our own investigation.

Our results are set forth in the table.

The data of the table fully confirm those characteristics of the course of the reaction between organomagnesium compounds and acid chlorides that we had established in previous investigations [1,2]; they also provide evidence that the method in question is highly suitable for the synthesis of alkoxyl-containing ketones.

EXPERIMENTAL

(In collaboration with I. G. Bilgildeeva, A. A. Vyatkina, V. Ya. Vlasova, G. V. Shilova and G. V. Maksimova)

1. Reaction of β-methoxy-α-naphthyl magnesium bromide with benzoyl chloride (1:1 ratio). Reactants: 29.6 g ($\frac{1}{8}$ mole) α-bromo-β-methoxynaphthalene, 4 g magnesium and 17.5 g ($\frac{1}{8}$ mole) benzoyl chloride.

Since β-methoxy-α-naphthyl magnesium bromide is relatively poorly soluble in absolute ether, it was synthesized in a mixture of ether and toluene (1:1). To the benzoyl chloride dissolved in toluene was added dropwise, with cooling and stirring, the ether-toluene solution of α-methoxy-β-naphthyl magnesium bromide. The mixture was heated for an hour. In order to avoid cleavage of the methoxyl group under the action of hydrochloric acid, saponification of the residual acid chloride was effected not with water but with 10% sodium carbonate solution. Heating with sodium carbonate was carried out for 30 minutes. The ether-toluene layer was separated from the aqueous layer, washed with water until neutral, and dried with sodium sulfate.

The mixture of compounds remaining behind after distilling off the solvent was distilled in vacuum. A second distillation of the main fraction (220-280° at 8 mm) gave 11 g of phenyl-(β-methoxy-α-naphthyl)-ketone (34% yield). B.p. 240-242° at 7 mm; m.p. 125-126° (from ligroin).

0.1390 g substance: 0.4190 g CO_2; 0.0670 g H_2O. 0.1398 g substance: 0.1170 g AgI. Found %: C 82.26; H 5.39; OCH_3 11.06. $C_{18}H_{14}O_2$. Calculated %: C 82.42; H 5.38; OCH_3 11.83.

An increase in the amount of organomagnesium compound to a 2:1 ratio brought the yield of ketone to 68%.

In the literature [6] the m.p. of phenyl-(β-methoxy-α-naphthyl)-ketone is given as 125°.

2. Reaction of β-ethoxy-α-naphthyl magnesium bromide with benzoyl chloride (2:1 ratio). The reactants were 31.1 g ($\frac{1}{8}$ mole) α-bromo-β-ethoxynaphthalene, 4 g magnesium and 8.8 g ($\frac{1}{16}$ mole) benzoyl chloride.

Reaction conditions were the same as in the preceding experiment except that the order of mixing of the components was changed, the ethereal solution of benzoyl chloride being added to the ethereal solution of the organomagnesium compound.

TABLE

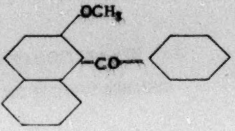
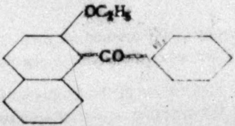
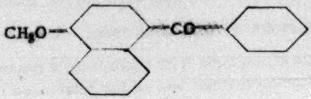
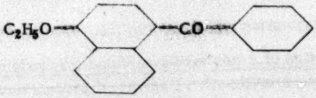
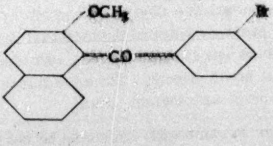
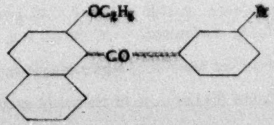
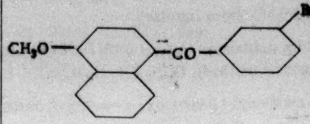
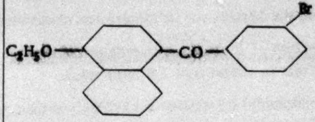
Prep. No.	Reaction components	Ratio of components	Formula of ketone	Yield of ketone (%)
1	β-Methoxy-α-naphthyl magnesium bromide + benzoyl chloride	1:1	 Phenyl-[β-methoxy-α-naphthyl]-ketone	34
2	The same	2:1	The same	68
3	β-Ethoxy-α-naphthyl magnesium bromide + benzoyl chloride	2:1	 Phenyl-[β-ethoxy-α-naphthyl]-ketone	70
4	4-Methoxy-1-naphthyl magnesium bromide + benzoyl chloride	1:1	 Phenyl-[4-methoxy-1-naphthyl]- ketone	52
5	4-Ethoxy-1-naphthyl magnesium bromide + benzoyl chloride	1:1	 Phenyl-[4-ethoxy-1-naphthyl]-ketone	50
6	β-Methoxy-α-naphthyl magnesium bromide + m-bromobenzoyl chloride	1:1	 m-Bromophenyl-[β-methoxy-α-naphthyl]-ketone	48
7	β-Ethoxy-α-naphthyl magnesium bromide + m-bromobenzoyl chloride	1:1	 m-Bromophenyl-[β-ethoxy-α-naphthyl]-ketone	50

TABLE (continued)

Prep. No.	Reaction components	Ratio of components	Formula of ketone	Yield of ketone (%)
8	4-Methoxy-1-naphthyl magnesium bromide + m-bromobenzoyl chloride	1:1	 m-Bromophenyl-[4-methoxy-1-naphthyl]-ketone	55
9	4-Ethoxy-1-naphthyl magnesium bromide + m-bromobenzoyl chloride	1:1	 m-Bromophenyl-[4-ethoxy-1-naphthyl]-ketone	56

Phenyl-(β-ethoxy-α-naphthyl)-ketone was isolated in the amount of 12 g (70 %). B.p. 211-212° at 2 mm; m.p. 79-80° (from ligroine).

0.1406 g substance: 0.4242 g CO_2; 0.0710 g H_2O; 0.1572 g substance: 0.1708 g AgI. Found %: C 82.72; H 5.65; OC_2H_5 14.4. $C_{19}H_{16}O_2$. Calculated %: C 82.58; H 5.83; OC_2H_5 16.3

This ketone has not been described in the literature.

3. Reaction of 4-methoxy-1-naphthyl magnesium bromide with benzoyl chloride (1:1) ratio. Starting materials: 39.5 g (1/6 mole) 1-bromo-4-methoxynaphthalene, 5 g magnesium and 23.4 g (1/6 mole) benzoyl chloride.

Reaction conditions were as in the first experiment.

The main fraction (220-240° at 7 mm) weighed 26 g. A second distillation of the main fraction gave 23 g (52 %) phenyl-(4-methoxy-1-naphthyl)-ketone. B.p. 213-215° at 4 mm; m.p. 81-82° (from a mixture of ligroine and toluene).

0.1136 g substance: 0.3425 g CO_2; 0.0530 g H_2O. 0.1252 g substance: 0.1065 g AgI. Found %: C 82.27; H 5.22; OCH_3 11.24. $C_{18}H_{14}O_2$. Calculated %: C 82.42; H 5.38; OCH_3 11.83.

In the literature the m.p. of this ketone [7] is given as 82-83°.

4. Reaction of 4-ethoxy-1-naphthyl magnesium bromide with benzoyl chloride (1:1 ratio). Starting substances: 41.8 g (1/6 mole) 1-bromo-4-ethoxynaphthalene, 5 g magnesium and 23.4 g (1/6 mole) benzoyl chloride.

The mixture of substances obtained in the reaction (carried out under the conditions of the first experiment) was distilled in vacuum at 8 mm: first fraction to 215 °; second fraction 215-260°, 25 g; residue in flask 3 g. A second distillation of the second fraction gave 23 g (50 %) phenyl-(4-ethoxy-1-naphthyl)-ketone. B.p. 245-247° at 8 mm; m.p. 71-72° (from ligroine + toluene).

0.0955 g substance: 0.3004 g CO_2; 0.0511 g H_2O. 0.1335 g substance: 0.1099 g AgI. Found %: C 82.37; H 5.74; OC_2H_5 16.16. $C_{19}H_{16}O_2$. Calculated %: C 82.58; H 5.83; OC_2H_5 16.30.

Phenyl-(4-ethoxy-1-naphthyl)ketone has a m.p. of 74-75° according to the literature [8].

5. Reaction of β-methoxy-α-naphthyl magnesium bromide with m-bromobenzoyl chloride (1: 1 ratio).

The amounts of starting materials were each 1/8 mole.

Reaction conditions were as in the first experiment.

The yield of m-bromophenyl-(β-methoxy-α-naphthyl)-ketone was 48% (20.5 g). B.p. 250-253° at 6 mm; m.p. 99-100° (from ligroine).

0.1565 g substance: 4.6 ml 0.1N $AgNO_3$. 0.2404 g substance: 0.1550 g AgI. Found %: Br 23.49 (Stepanov's method); OCH_3 8.5. $C_{18}H_{13}O_2Br$. Calculated %: Br 23.42; OCH_3 9.1.

m-Bromophenyl-(β-methoxy-α-naphthyl)-ketone forms a picrate with m.p. 114-115°.

0.0445 g substance: 2.3 ml 0.1 N HCl (hydrogenation by Ter Meulen method). Found %: N 7.24. $C_{24}H_{16}O_9N_3Br$. Calculated %: N 7.36.

Neither the ketone nor its picrate are mentioned in the literature.

6. Reaction of β-ethoxy-α-naphthyl magnesium bromide with m-bromobenzoyl chloride (1:1 ratio).

Starting materials in amounts of 1/8 mole each.

m-Bromophenyl-(β-ethoxy-α-naphthyl)-ketone partly decomposes when distilled in vacuum; after removal of solvent, it was therefore isolated from the reaction mixture by freezing. M.p. 97-98° (from ligroine). Yield 22 g (50%).

0.1811 g substance: 5.1 ml 0.1 N $AgNO_3$ (Stepanov's method). 0.1529 g substance: 0.0948 g AgI. Found %: Br 22.50; OC_2H_5 11.91. $C_{19}H_{15}O_2Br$. Calculated %: Br 22.50; OC_2H_5 12.68.

This ketone is likewise not described in the literature.

7. Reaction of 4-methoxy-1-naphthyl magnesium bromide with m-bromobenzoyl chloride (1:1 ratio).

Reaction components were 34.0 g (1/7 mole) 1-bromo-4-methoxynaphthalene, 5 g magnesium and 31.3 g (1/7 mole) m-bromobenzoyl chloride.

Vacuum distillation (8 mm) of the reaction product gave the following fractions: I) up to 205°; II) 205-206°, 30 g; residue in flask 1 g. A second distillation of the second fraction gave 27 g (55%) of m-bromophenyl-(4-methoxy-1-naphthyl)-ketone. B.p. 244-245° at 5 mm; m.p. 129° (from ligroine-toluene mixture).

0.1001 g substance: 0.0546 g AgBr 0.0814 g substance: 2.3 ml 0.1 N $AgNO_3$. Found %: Br 23.20; OCH_3 8.8. $C_{18}H_{13}O_2Br$. Calculated %: Br 23.42; OCH_3 9.1.

m-Bromophenyl-(4-methoxy-1-naphthyl)-ketone is not described in the literature.

8. Reaction of 4-ethoxy-1-naphthyl magnesium bromide with m-bromobenzoyl chloride (1:1 ratio).

Starting substances: 36.0 g (1/7 mole) 1-bromo-4-ethoxynaphthalene, 5 g magnesium and 31.3 g (1/7 mole) m-bromobenzoyl chloride.

The yield of m-bromophenyl-(4-ethoxy-1-naphthyl)-ketone was 28 g (56%). M.p. 95-96° (from ligroine-toluene mixture).

0.0967 g substance: 2.7 ml 0.1 N $AgNO_3$ (Stepanov's method). 0.1033 g substance: 2.8 ml 0.1 N $AgNO_3$ (Kirpal method). Found %: Br 22.28; OC_2H_5 12.21. $C_{19}H_{15}O_2Br$. Calculated %: Br 22.50; OC_2H_5 12.68.

This ketone has not previously been reported in the literature.

SUMMARY

1. The research described in this paper demonstrates the possibility of synthesis of ketones by the reaction of organomagnesium compounds with acid chlorides even in more complicated cases when the reactants contain various alkoxyl groups.

2. 8 Alkoxyl-containing ketones have been synthesized, of which 5 have not previously been described in the literature.

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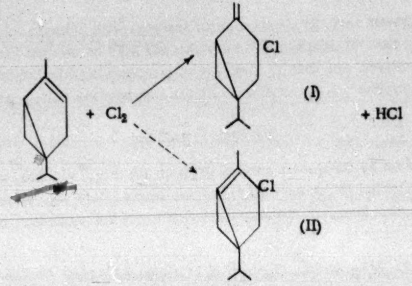
**See Consultants Bureau Translation, p. 1411.

NEW TYPES OF TERPENE TRANSFORMATIONS

XIII. THE ACTION OF CHLORINE ON α-THUJENE

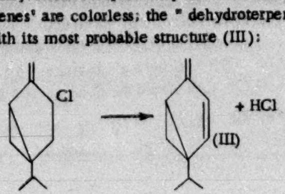
D. Tishchenko and T. Danilova

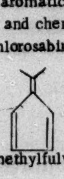
In Communication I general consideration was given to the characteristics of reaction of chlorine with terpenes [1], while in Communication V experimental data were presented for the action of chlorine on Δ^3-carene. It was found that in our chosen conditions the three-membered ring of carene does not react either with chlorine or with hydrogen chloride, and the primary product of the reaction is 3-chloro-Δ^4-carene. It was desirable to establish whether this case of stability of the three-membered ring in bicyclic terpenes was the rule or an exception. To this end we studied the action of chlorine on α-thujene. α-Thujene is an analog of trimethylethylene, and hence Lvov's reaction should proceed for it with a sufficiently high yield, although lower than for trimethylethylene (about 90%), due to the "hemicyclic prohibition"; another direction of the reaction is improbable due to the "Bredt prohibition:"



Chloride (I) should be stable at 70°, and on ozonization it should give formaldehyde (or formic acid) and a chloroketone of the composition $C_9H_{13}OCl$. Chloride (II) on ozonization will give a chlorodiketone $C_{10}H_{15}O_2Cl$. Ozonization gave a chloroketone, thus establishing structure (I) for the chloride of α-thujene (2-chlorosabinene). Cleavage by chlorine of the three-membered ring should give a monochloride with two double bonds, which would exclude the possibility of obtaining the chloroketone $C_9H_{13}OCl$. It was thus shown that the case of Δ^3-carene is not exceptional and that the three-membered ring in bicyclic terpenes is stable in our chosen chlorination conditions.

We brought chloride (I) into reaction with potassium acetate; apart from the expected ester of terpenol, there was obtained a substance which was bright-red both as vapor and liquid and whose constants corresponded to a hydrocarbon $C_{10}H_{14}$ ("dehydroterpene"). We obtained these "dehydroterpenes" by removing a molecule of hydrogen chloride from the monochlorides of terpinolene, carene and β-pyronene. In composition they correspond to tetramethylbenzenes and other isomers of aromatic hydrocarbons of the composition $C_{10}H_{14}$, but they differ conspicuously from the latter in physical and chemical properties. The latter three "dehydroterpenes" are colorless; the "dehydroterpene" from 2-chlorosabinene is colored, which fact is fully consistent with its most probable structure (III):





Dimethylfulvene

This structure of 2,7-sabinadiene emphasizes its analogy with the colored fulvenes, hydrocarbons with a crossed system of conjugated double bonds. If we assume that it contains a three-membered ring without a multiple bond. The other possible structure of 1,7-sabinadiene with an allenic grouping is very much less probable both from thermodynamic considerations and from the fact that our "dehydroterpene" is colored. Allenic hydrocarbons are colorless. We established that the "dehydroterpene" from terpinolene chloride corresponds to the structure 1,3,8(9)-p-menthatriene, and the "dehydroterpene" from carene chloride to 2,4-caradiene. They are both isomeric with 2,7-sabinadiene, and of course with p-cymene, and their isomerization to p-cymene ought to be accompanied by very considerable release of energy ("ring aromatization"). This isomerization, however, does not take place either on formation of "dehydroterpenes" or during their isolation and purification. These facts throw doubt on the now fairly widespread views of the structure of systems of conjugated double bonds. The theory is that in such systems the valence electrons are not firmly anchored between the respective atoms and can move fairly freely throughout the whole system, "creating a different density of electron cloud at different points". Such a "mobility of the electron cloud" should greatly facilitate, thermochemically, advantageous isomerization reactions, as in our case for instance. In actual fact, "dehydroterpenes" are fairly stable. We are forced to the conclusion that the ideas about "mobility of the electron cloud in a system of conjugated double bonds", in our case at least, do not accord with the facts.

We did not prove the structure of terpenol, prepared by reaction of potassium acetate with 2-chlorosabinene. It can be either 2-hydroxysabinene or 7-hydroxy-α-thujene (allyl rearrangement in the instant of the ion-exchange reaction).

This investigation showed that the mechanism of reaction with chlorine advanced by us in Communication I is also valid for α-thujene, that the resultant 2-chlorosabinene may be brought into anion exchange reaction to give the corresponding derivatives, and that by cleavage of a molecule of hydrogen chloride it is converted into an orange-colored "dehydroterpene", a hydrocarbon with the composition $C_{10}H_{14}$, apparently 2,7-sabinadiene.

EXPERIMENTAL

α-Thujene was prepared by Chugaev's method [2] from DL-thujyl alcohol, which we obtained from β-thujone by reduction with isopropyl alcohol in presence of aluminum isopropylate [4]. Rectification of the mixture of hydrocarbons in a column with an efficiency of 40 theoretical plates yielded a constant boiling fraction identified as α-thujene with b.p. 49-50° at 21 mm.

d_4^{20} 0.829; n_D^{20} 1.4512; MR_D 44.22. $C_{10}H_{16}\digamma\triangle$. Calculated 44.21.

Chlorination was performed in conditions which have often been described. Reagents were α-thujene 111 g, $KMnO_4$ 30 g, HCl (1.19) 120 ml, sodium bicarbonate 100 g. The organic products of reaction weighed 126.9 g and contained 18.46 g chlorine. The inorganic chlorine content was 10.11 g; per cent anomalous reaction = 70.8.

The reaction product was fractionated in a column of 6-7 theoretical plates and at a bath temperature not higher than 70°. The main fraction of monochloride had b.p. 37° at 0.17 mm.

d_4^{20} 0.984; n_D^{20} 1.4862; MR_D 49.78; $C_{10}H_{15}Cl\digamma\triangle$. Calculated 49.08.

The exaltation of refraction (0.7) is exactly characteristic of the hemicyclic double bond conjugated with a three-membered ring.

0.1424, 0.1704 g substance: 0.1132, 0.1372 g AgCl. Found %: Cl 19.7, 20.9. $C_{10}H_{15}Cl$. Calculated %: Cl 20.8. Allylic chlorine was found by digesting a weighed sample with potassium acetate in acetic acid: 19.3 and 19.3%.

Ozonization of the monochloride. 10 g monochloride in 80 ml chloroform was ozonized with 78 liters of 5% ozone. The chloroform was removed from a tenth part of the solution of the ozonide in vacuum. Residue was a viscous liquid weighing 1.3 g.

0.2014 g substance: 0.4026 g CO_2; 0.1298 g H_2O. 0.2203, 0.1418 g substance: 0.1472, 0.0960 g AgCl. Found %: C 54.5; H 7.2; Cl 16.5, 16.7. $C_{10}H_{15}O_3Cl$. Calculated %: C 54.9; H 6.9; Cl 16.2.

The remaining ozonide solution was hydrolyzed by slow addition to boiling water, while the hydrolysis products were distilled off. In the aqueous layer was found 0.6 mole formic acid and 0.3 mole formaldehyde (isolated as formal-dimedone).

The chloroform was driven out of the chloroform layer; the weight of the residue was 6.5 g; it was fractionated at 0.1 mm. The principal fraction (3.9 g) melted at 86-88°.

d_4^{20} 1.105; n_D^{20} 1.4896; MR_D 45.1; $C_9H_{13}OCl\,\Delta$ (chloroketone). Calculated: 44.94.

0.1197, 0.1272 g substance: 0.2731, 0.2908 g CO_2; 0.0852, 0.0916 g H_2O. 0.1015, 0.1747 g substance: 0.0800, 0.1392 g AgCl. Found %: C 62.2, 62.3; H 8.0, 8.1; Cl 19.5, 19.7. $C_9H_{13}OCl$. Calculated %: C 62.7; H 7.5; Cl 20.5.

Oxidation of the chloroketone. 0.9 g was oxidized with a solution of 0.2 g permanganate. The isolated crystalline acid with m.p. about 140° was transformed into the silver salt.

Found %: Ag 53.1, 52.6. $C_9H_{12}O_4Ag_2$. Calculated %: Ag 53.9.

Preparation of the semicarbazone. To a solution of 0.4 g chloroketone in alcohol was added an aqueous solution of 0.4 g potassium acetate and 0.4 g semicarbazide hydrochloride. The resultant precipitate was dissolved in alcohol with heating. Crystals came down after 3 days and were washed in alcohol and dried. M.p. 220°; no chlorine present. Its analysis corresponded closest of all to the semicarbazido-semicarbazone $C_{11}H_{20}O_2N_6$.

Found %: N 27.5, 27.8. $C_{11}H_{20}O_2N_6$. Calculated %: N 31.3.

Reaction of 2-chlorosabinene with potassium acetate. 14.5 g monochloride, 13 g of the salt and 10 g acetic acid were heated 4 hours on a water bath and then 2 hours on a sand bath at the boil. After cooling, the solution was diluted with three times the volume of water and extracted with ligroine. In the aqueous layer was found 5.6 g chlorine; the reaction took place to the extent of 90%. The solvent was removed from the extract; weight of residue 15.4 g; it was fractionated in a small column and gave two main fractions: 1) b.p. 40-41° at 5 mm (yield about 30% of the possible); 2) b.p. 74.6° at 2 mm (yield about 30% of the possible).

Fraction 1) was a mobile, dark-orange liquid; the vapor had the same color:

d_4^{20} 0.855, n_D^{20} 1.4860; MR_D 45.5. $C_{10}H_{14}\,\overline{|}_2\,\Delta$. Calculated 43.75.

0.0632, 0.0534 g substance: 0.2080, 0.1752 g CO_2; 0.0655, 0.0556 g H_2O. Found %: C 89.7, 89.5; H 11.6, 11.7. $C_{10}H_{14}$. Calculated %: C 89.55, H 10.45.

The total % of C and H = 101.2. The combustion analysis for benzoic acid gave a systematic error for hydrogen of the order of +0.6 to +0.7%. With this correction the analytical figures are acceptable and correspond to the composition $C_{10}H_{14}$.

The hydrocarbon is decolorized when its benzene solution is heated with maleic anhydride.

Fraction 2) is colorless.

d_4^{20} 0.969; n_D^{20} 1.47065; MR_D 55.94. $C_{10}H_{15}OCOCH_3\,\overset{=}{|}\,\Delta$. Calculated: 55.10.

Saponification number: found 282, calculated 288.

Preparation of the alcohol. 2.3 g fraction 2) was heated on a bath for 2 hours with a solution of 1 g KOH in 50 ml alcohol. The reaction product had an orange color. The solution was diluted with three times the volume of water and extracted with ligroine. The solvent was driven off from the extract and the residue fractionated at 3 mm. The first runnings were colored orange ("dehydroterpene"); at 66-68° the anticipated terpenol came over (1.2g).

d_4^{20} 0.942; n_D^{20} 1.4861; MR_D 46.33. $C_{10}H_{16}O\,\overline{|}\,\Delta$. Calculated 45.74.

Found %: OH 10.5, 10.7. (Chugaev-Tserevitinov). $C_{10}H_{16}O$. Calculated %: OH 11.2.

Semmler [3] gives for sabinol d_4^{20} 0.943; n_D^{20} 1.488.

SUMMARY

1. The action of chlorine on α-thujene was investigated.

2. In accord with the considerations developed in Communication I, the main product of the reaction is 2-chlorosabinene.

3. Reaction of 2-chlorosabinene with potassium acetate leads to the ester of terpenol and dark-orange "dehydroterpene" $C_{10}H_{14}$, probably 2,7-sabinadiene, an analog of the fulvenes.

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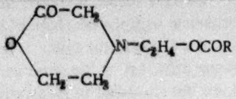
* See Consultants Bureau English translation, page 593.

SYNTHESIS AND TRANSFORMATIONS OF SOME DERIVATIVES OF N,N-DI-(β-HYDROXYETHYL)-AMINOACETIC ACID

II. ESTERS OF N,N-DIHYDROXYETHYLAMINOACETIC ACID AND N-HYDROXYETHYLMORPHOLONE

N. V. Khromov and A. L. Remizov

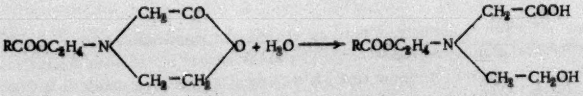
In the previous communication [1] it was pointed out that the dehydration of N,N-di-(β-hydroxyethyl)-aminoacetic acid in presence of hydrochloric acid leads to formation of the hydrochloride of N-(β-hydroxyethyl)-morpholone-2. Consistent with this structure of the compound is the complete identity of its acetyl, benzoyl and diphenylacetyl derivatives (esters) with the acetic (I), benzoic (II) and diphenylacetic (III) esters of N-hydroxyethylmorpholone synthesized from the latter when reacted in the form of the free base.



R = CH_3; C_6H_5; $(C_6H_5)_2CH$
(I) (II) (III)

Preparation of the esters both from the hydrochloride and from hydroxyethylmorpholone base was effected with the help of the acid chlorides of the corresponding acids in a medium of pyridine. None of the three esters is described in the literature. They are glycerol-like liquids with very weak basic properties. The hydrochlorides of the esters proved to be unstable (they deliquesced in the air and dissociated even when heated gently); they were therefore identified through the picrates and picrolonates. The picrate and picrolonate of acetate (I), the picrate of benzoate (II), and the picrolonate of diphenylacetate (III) were prepared for this purpose. The last-named ester had such feeble basic properties that it did not form a stable picrate. Even the picrolonate was distinguished by lability and decomposed on crystyllization.

In the same way as hydroxyethylmorpholone on hydrolysis gives dihydroxyethylaminoacetic acid, so also the synthesized cyclic esters on heating with water are transformed into the corresponding acids by the reaction:



R = CH_3; C_6H_5; $(C_6H_5)_2CH$.
(IV) (V) (VI)

The acids (IV, V, VI,) prepared in this way are monoesters of dihydroxyethlglycine; they are crystalline substances. During melting they lose water to form the original esters of hydroxyethylmorpholone; once melted, therefore, they do not solidify on cooling and in all their physical and chemical properties (solubility, formation of picrates and pricrolonates) they become perfectly identical with the corresponding esters of hydroxyethylmorpholone.

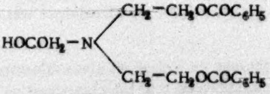
In solutions containing water, both forms of the esters (the acidic and the lactone) apparently exist in equilibrium which with rising temperature is shifted in the direction of closure of the lactone ring, as can be conveniently observed in the case of the aqueous solution of the monobenzoate of dihydroxyethylglycine (V). This compound is notable for its high solubility in water, whereas the benzoate of hydroxyethylmorpholone (II) formed from it is almost insoluble in water. If the aqueous solution of the open-chain form is evaporated on the water bath to a very small volume and then diluted with water, the liquid separates into two layers: an upper one aqueous and a lower oily one. In all its properties the oil is identical with the benzoate of hydroxyethylmorpholone.

Consequently the process of opening of the lactone ring even proceeds in aqueous solutions. This is also demonstrated by the fact that after evaporation of the solvent (aqueous methanol or ethanol) from the mother liquor obtained on recrystallizing the dihydroxyethylglycine monobenzoate a gelatinous mass remains which, unlike the original crystalline product, is soluble in benzene and similar solvents and forms a picrate which does not differ from the picrate of hydroxyethylmorpholone benzoate. No matter how pure is the open ester taken for crystallization, the mother liquor will always contain the lactone. In this case also, therefore, an equilibrium is established between the hydroxy acid and its lactone.

An attempt was made to synthesize the monobenzoate of dihydroxyethylglycine directly from the dihydroxy acid. The reaction was carried out between benzoyl chloride and dihydroxyethylglycine in a pyridine medium, using a molar ratio of 1:1. In place, however, of the monoester of the dihydroxy acid which should have been obtained in the normal course of the reaction, the original dihydroxyethylglycine was recovered from the reaction mixture (nearly 40% of the original amount was recovered), and benzoic acid and hydroxyethylmorpholone benzoate were also formed.

A similar attempt to synthesize the dibenzoate from dihydroxyethylglycine and two molecules of benzoyl chloride (in pyridine) was also unsuccessful. In this case again, instead of the anticipated dibenzoyl derivative, the benzoate of hydroxyethylmorpholone was obtained. Such a course of the benzoylation of dihydroxyethylglycine becomes intelligible if we assume the following mechanism. The first step is the normal process of esterification to form the monobenzoate of dihydroxyethylglycine(V). We have shown, however, that the monobenzoate of dihydroxyethylglycine in solution (especially when hot) is in equilibrium with the benzoate of hydroxyethylmorpholone (II). Since the benzoyl chloride-pyridine complex is know to avidly absorb water, the latter is progressively removed from the sphere of reaction. The equilibrium is consequently shifted to the right, i.e. in the direction of formation of the morpholone derivative, as we also observed in our experiments. Hence the sole route to preparation of the monoesters of dihydroxyethylglycine lies through the step of isolation of the esters of hydroxyethylmorpholones followed by their hydrolysis.

The dibenzoate of dihydroxyethylglycine could only be prepared by benzoylation in an alkaline medium (Schotten-Baumann). It proved to be not identical in properties with the compound synthesized by an analogous method by Kiprianov [2]; this compound, according to Kiprianov, was a soft, easily fusible mass which formed a benzoylethyl ester when recrystallized from alcohol. The dibenzoyl derivative of dihydroxyethylglycine that we prepared had a well-defined crystalline structure, melted sharply at 142° and did not undergo any decomposition when recrystallized from methanol or ethanol. Its structure as the dibenzoate of dihydroyxethylglycine (VII) was confirmed by the elementary analysis -and by all its properties. As shown by our observations, the tendency of monoesters of dihydroxyethylglycine to change into the lactone is in definite relation to the degree of basicity of the formed morpholone derivatives. The weaker the basic properties of the cyclic product, the more easily is it formed and the more stable it is. Such a relation between the stability of morpholone derivatives and their basicity is conspicuous when we compare the properties of hydroxyethylmorpholone and its esters.



$$\mathrm{HOCOH_2{-}N}\begin{cases}\mathrm{CH_2{-}CH_2OCOC_6H_5}\\ \mathrm{CH_2{-}CH_2OCOC_6H_5}\end{cases}$$

(VII)

The basic properties of hydroxyethylmorpholone are fairly well marked. Its aqueous solutions have a weakly alkaline reaction to Brilliant Yellow paper (pH about 7.5); the hydrochloride is quite stable in the crystalline form and does not undergo appreciable dissociation on prolonged heating at temperatures not higher than its melting point (139°).

By contrast, hydroxyethylmorpholone has poor stability in the form of its free base: after only a few days in the air, it is covered with a dense crust of dihydroxyethylglycine due to hydrolysis. The basic properties and stability of esters of hydroxyethylmorpholone are in marked contrast. All of the three esters which we have studied (acetate, benzoate and diphenylacetate) possess negligible basicity. Their aqueous solutions (admittedly very dilute) have a neutral reaction to all the usual indicators with a color change in the pH range of 5 to 7 (e.g. methyl red and litmus). Attention has been drawn above to the instability of their hydrochlorides. Note has also been made of the extraordinarily low basicity of the diphenylacetate, which does not even form a picrate. On the other hand, the esters of hydroxyethylmorpholone are much more stable than the original amino alcohol and can be exposed to the air without appreciable hydrolysis over a period of days. The diphenylacetate is particularly stable, which is fully consistent with its very low basicity. The same considerations may be said to apply to the ease of closure of the morpholone ring. Here a convenient criterion is the melting point of dihydroxyethylglycine and its monoesters, since this temperature is essentially not only the point of change of physical state but is also to a great extent the point of transformation of the hydroxy acid into its lactone (accompanied by closure of the morpholone ring). The lower the melting point of the compound in question, the more easily (in otherwise identical conditions) is the morpholone derivative formed.

In the table below are listed the "melting" points of dihdroxyethylglycine and of its three monoesters.

Substance		Temperature of transformation* into lactone
Dihydroxyethylglycine		190-192°
"	monoacetate	102-104
"	monobenzoate	127-127.5
"	diphenylacetate	82-84

The data in the table show that dihydroxyethylglycine changes into the morpholone derivative much less readily than its monoesters. Of the latter the diphenylacetate forms the lactone with the greatest ease. The basic properties of the diphenylacetate, as repeatedly observed, are the weakest of all the esters. Such a correlation between the basicity of the morpholones and their stability is also in accord with the fact that N,N-arylhydroxyethylglycines generally cannot be obtained in the free state, because they are transformed into the corresponding N-arylmorpholones on simple acidification of solutions of their salts. Yet for the purpose of cyclization of the N,N-alkylhydroxyethlglycines it is necessary to have recourse to dry distillation in vacuum, the resultant alkylmorpholones being readily hydrolyzed with transformation into the original acids [3].

EXPERIMENTAL

Benzoate of N-hydroxyethylmorpholone. 3.36 g (0.023 mole) freshly distilled hydroxyethylmorpholone or 4.18 g of its hydrochloride was dissolved in twice the volume of dry pyridine, and to the cooled (ice water) pyridine solution was slowly added (with energetic shaking) from a dropping funnel benzoyl chloride in the amount of 3.3 g (0.0235 mole), and the residue in the funnel washed out with 0.5 ml dry benzene. The reaction flask was fitted with an air condenser and protected in the usual manner against access of atmospheric moisture. The mixture was heated on the water bath for 2-3 hours, after which it was cooled and the formed viscous crystalline mass was diluted with dry xylene. The xylene-pyridine solution was filtered from the precipitate of pyridine hydrochloride and evaporated to a very small volume in vacuum. The residue was diluted with dry xylene; the solution was filtered (if necessary) and again evaporated down in vacuum. The residue was dissolved in benzene, dried over BaO and, after distillation of the benzene, distilled in vacuum. The yield of fraction with b.p. 210-212° at 3.5 mm was 4.0-4.2 g or 69-72%/of the theoretical. This is a glycerol-like, colorless liquid, soluble in aromatic hydrocarbons, ether and all polar solvents, but poorly soluble in water. When kept in an open vessel for several weeks, it gradually hydrolyzes to form the monobenzoate of dihydroxyethylglycine.

0.1946 g substance: 0.4454 g CO_2; 0.1096 g H_2O 0.1520 g substance: 0.3486 g CO_2; 0.0842 g H_2O. 0.3726 g substance 18.0 ml N_2 (24°, 766 mm). 0.3212 g substance: 15.7 ml N_2 (24°, 763 mm).
Found %: C 62.46, 62.58; H 6.30, 6.20; N 5.59, 5.64. $C_{13}H_{15}O_4N$. Calculated %: C 62.66; H 6.07; N 5.62.

Picrate of the benzoate of N-hydroxyethylmorpholone. Prepared by mixing equimolar amounts of hot benzene solutions of the ester and picric acid. The picrate forms bright-yellow, elongated, acicular prisms (from glacial acetic acid + acetone). M.p. 204-206° (with decomposition). Soluble in water, acetone and glacial acetic acid, poorly soluble in methanol and ethanol. Insoluble in nonpolar solvents.

0.1054 g substance: 0.1842 g CO_2; 0.0360 g H_2O. 0.1104 g substance: 0.1918 g CO_2; 0.0352 g H_2O. 0.1390 g substance: 14.6 ml N_2 (24°, 743 mm). 0.1494 g substance: 16.0 ml N_2 (25°, 738 mm).
Found %: C 47.69, 47.41; H 3.82, 3.57; N 11.81, 11.92. $C_{19}H_{18}O_{11}N_4$. Calculated %: C 47.70; H 3.79; N 11.71.

Monobenzoate of dihydroxyethylglycine. 2.5 g distilled hydroxyethylmorpholone benzoate was mixed with 5 ml water and heated on the water bath until the boundary between the layers of oil and water had disappeared. The residue was diluted with water (this caused the oil to separate again) and again evaporated on the water bath until a thick, gelatinous mass had formed; this was cooled (ice bath) and seeded; after a few hours it crystallized. The so-obtained solid product was pulverized, treated with acetone and pressed on the filter. Yield 1.85-2.0 g or 80-85% of the theoretical. After recrystallization from methanol or ethanol (preferably with acetone) the substance melted at 127-127.5° (on heating the capillary, starting at 120°) and formed colorless needles (under the microscope). It is highly soluble in water, hot methanol, ethanol and glacial acetic acid; moderately soluble in cold methanol and ethanol; still less soluble in acetone. Its solubility in nonpolar solvents is negligible. No matter how pure was the initial monobenzoate of the dihydroxy acid, the alcoholic mother liquors, after their crystallization, always contained the benzoate of hydroxyethylmorpholone, since, after evaporation of the alcohol (in the air), an oil remained which gave a picrate with an m.p. 200-204°, identical with hydroxyethylmorpholone benzoate picrate (mixed m.p. 202-205°).

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* Here, as elsewhere in the text, the temperatures have been corrected for the exposed stem of the thermometer.

0.0782 g substance: 0.1680 g CO_2; 0.0448 g H_2O. 0.1444 g substance: 0.3085 g CO_2; 0.0854 g H_2O. 0.1692 g substance: 8.0 ml N_2 (24°, 750 mm). 0.2710 g substance: 12.6 ml N_2 (23°, 761 mm). Found %: C 58.63, 58.30; H 6.41, 6.62; N 5.36, 5.37. $C_{13}H_{17}O_5N$. Calculated %: C 58.41; H 6.41; N 5.24.

Attempt to prepare the monobenzoate of dihydroxyethylglycine from dihydroxyethylglycine and benzoyl chloride. To 1.63 g (0.01 mole) dihydroxyethylglycine in 10 ml dry pyridine was added dropwise 1.41 g (0.01 mole) benzoyl chloride. The amount of solid dihydroxyethylglycine appreciably lessened. The mixture was heated on the water bath (in a flask fitted with an air condenser and a calcium chloride tube) for 3 hours, after which it was cooled and the pyridine solution was poured off from the insoluble pasty, resinous, colorless mass which remained at the bottom of the reaction flask. The pyridine solution was diluted with twice the volume of dry xylene, filtered from the precipitate of pyridine hydrochloride and evaporated down in vacuum. The residue after evaporation was diluted with xylene and again evaporated. The resultant thick, crystalline slurry was carefully treated with cold benzene and the benzene extract was mixed with a benzene solution of picric acid. A precipitate of the picrate of hydroxyethylmorpholone with m.p. 203-205° was obtained (mixed m.p. 204-206°). The benzene-insoluble crystalline precipitate of benzoic acid was recrystallized from aqueous alcohol. M.p. 120°. A mixed sample with benzoic acid melted at 120-121°. The resinous material remaining in the flask was treated with absolute alcohol to give a white crystalline precipitate with m.p. 175-178°, weight 0.64 g. After recrystallization from 80% methanol it melted at 186-189°. A mixture with dihydroxyethylglycine melted at 184-190°. Consequently, the treatment of dihydroxyethylglycine with an equimolar amount of benzoyl chloride resulted in formation of the benzoate of hydroxyethylmorpholone. Half of the original benzoyl chloride was separated by addition of water and was converted into benzoic acid. Correspondingly, one half of the original dihydroxyethylglycine remained unchanged.

Attempt to prepare the dibenzoate of dihydroxyethylglycine from dihydroxyethylglycine and benzoyl chloride. The reaction was performed as described above except that the molar ratio of dihydroxy acid and benzoyl chloride was 2:1. The actual quantities were 0.82 g (0.005 mole) dihydroxy acid and 1.42 g (0.01 mole) benzoyl chloride. Reaction products were hydroxyethylmorpholone benzoate (identified as the picrate) and benzoic acid. The original dihydroxyethylglycine could not be detected in the reaction mixture.

Dihydroxyethylglycine dibenzoate. To a solution of 1.63 g (0.01 mole) dihydroxyethylglycine in 5 ml water was added (with energetic shaking in a flask with a ground-glass stopper) alternately a 25% NaOH solution and benzoyl chloride in such a manner that the medium always remained alkaline to phenolphthalein and not too much unreacted benzoyl chloride accumulated. From time to time the reaction mixture was cooled to room temperature. In this manner a total of 13.0 ml 25% NaOH (0.081 mole) and 6.05 g (0.043 mole) benzoyl chloride was added. After the whole of the benzoyl chloride had entered into reaction (indicated by the disappearance of the oily drops), the perfectly homogeneous solution was carefully acidified with 10 N hydrochloric acid until weakly acid to litmus but not yet acid to Congo. The snow-white precipitate was filtered, well pressed on the filter and transferred to a beaker where it was triturated with 1-2 ml ethanol and 8-10 ml ether for purification from benzoic acid. The suspension was filtered, and the precipitate washed with ether. Yield 1.30-1.36 g or 70-73% of the theoretical. The substance crystallizes from methanol or ethanol in the form of long, soft needles resembling asbestos fiber; m.p. 141.5-142.5°. Readily soluble in acetone, benzene, chloroform, hot methanol and ethanol; less soluble in cold water and ether.

0.1268 g substance: 0.3006 g CO_2; 0.0680 g H_2O. 0.2032 g substance: 0.4796 g CO_2; 0.1068 g H_2O. 0.3120 g substance: 10.5 ml N_2 (22°, 740 mm). 0.6510 g substance: 21.5 ml N_2 (24°, 750 mm). Found %: C 64.69, 64.41; H 6.00, 5.88; N 3.79, 3.75. $C_{20}H_{21}O_6N$. Calculated %: C 64.67; H 5.70; N 3.77.

N-Hydroxyethylmorpholone acetate. 4.35 g (0.03 mole) hydroxyethylmorpholone or the equivalent amount of its hydrochloride, was dissolved in 2-3 times the volume of dry pyridine, and into the obtained solution was gradually run, while cooling and excluding atmospheric moisture (the reaction was carried out in a flask fitted with a dropping funnel and an air condenser with a calcium chloride tube), 1.5 g (0.019 mole) acetyl chloride. The mixture was then left at room temperature for 30-40 minutes and the reaction completed by heating for an hour on the water bath. The so-obtained dark-red (sometimes brownish-yellow) pyridine solution was cooled and formed a crystalline slurry which was diluted with twice the volume of dry xylene; the crystals of pyridine hydrochloride were separated by filtration. The filtrate was freed from pyridine by evaporation in vacuum; the residue from the evaporation was diluted with xylene and the precipitate was filtered off. The xylene was then distilled off in vacuum and the residue distilled at 5 mm to give a fraction at 165-171°. Yield 2.0-2.1 g or 63% of the theoretical. Properties: colorless liquid, boiling at 167-168° (5 mm residual pressure), readily soluble in water and all other common solvents except gasoline, carbon tetrachloride and ether.

0.1816 g substance: 0.3428 g CO_2; 0.1163 g H_2O. 0.1488 g substance: 0.2804 g CO_2; 0.0944 g H_2O. 0.2954 g substance: 18.8 ml N_2 (23°, 772 mm). 0.3258 g substance: 21.1 ml N_2 (24°, 775 mm).

Found %: C 51.51, 51.42; H 7.17, 7.10; N 7.46, 7.59. $C_8H_{13}O_4N$. Calculated %: C 51.33; H 7.00; N 7.48.

N-Hydroxyethylmorpholone acetate picrate. Prepared by mixing an alcoholic solution of the base with a hot concentrated benzene solution of the equivalent amount of picric acid. The oil formed crystallized rapidly. Yellow prisms (from acetone-methanol), sparingly soluble in common solvents excepting glacial acetic acid and acetone. M.p. 167-168°.

0.1778 g substance: 0.2639 g CO_2; 0.0624 g H_2O. 0.2212 g substance: 0.3298 g CO_2; 0.0788 g H_2O. 0.1266 g substance: 15.2 ml N_2 (24°, 755 mm). 0.1607 g substance: 19.4 ml N_2 (24°, 750 mm).

Found %: C 40.50, 40.69; H 3.93, 3.99; N 13.71, 13.69; $C_{14}H_{16}O_{11}N_4$. Calculated %: C 40.39; H 3.88; N 13.46.

Picrolonate of N-hydroxyethylmorpholone acetate. Prepared by mixing hot concentrated solutions in absolute alcohol of hydroxyethylmorpholone acetate and picrolonic acid (equimolecular amounts). The substance forms long yellow prisms (from glacial acetic acid), m.p. (with decomp.) 186-187.5°. Solubility like that of the picrate.

0.1556 g substance: 0.2751 g CO_2; 0.0666 g H_2O. 0.1500 g substance: 0.2645 g CO_2: 0.0637 g H_2O. 0.0934 g substance: 12.8 ml N_2 (24°, 760 mm). 0.1547 g substance: 20.7 ml N_2 (24°, 773 mm). Found %: C 48.29, 48.13; H 4.79, 4.75; N 15.75, 15.64. $C_{18}H_{21}O_9N$. Calculated %: C 47.89; H 4.69; N 15.53.

Monoacetate of N,N-dihydroxyethylglycine. 2 g N-hydroxyethylmorpholone acetate was dissolved in 10-15 ml water and the solution was evaporated on the water bath to a thick, yellowish syrup. Evaporation was then continued in vacuum (at the temperature of the boiling water bath) and the resultant resinous mass was kept in a vacuum desiccator over KOH until it solidified.

The solid, amorphous product was reduced to powder, treated with 4-5 ml boiling acetone, filtered from mother liquor, dried and recrystallized from methanol-acetone. M.p. 102.5-104°. Very soluble in water, lower alcohols and glacial acetic acid; poorly soluble in acetone and ether.

0.1550 g substance: 0.2660 g CO_2; 0.1030 g H_2O. 0.1740 g substance: 0.2986 g CO_2; 0.1160 g H_2O. 0.2630 g substance: 16.3 ml N_2 (24°, 754 mm). 0.2248 g substance: 13.5 ml N_2 (24°, 760 mm). Found %: C 46.83, 46.83; H 7.44, 7.46; N 7.07, 6.90. $C_8H_{15}O_5N$. Calculated %: C 46.82; H 7.37; N 6.83.

Partial diphenyl acetate of dihyroxyethylglycine. 1.9 g freshly distilled hydroxyethylmorpholone (0.0105 mole) was placed in a small flask fitted with an air condenser and a calcium chloride tube; 7 ml dry pyridine was added to the flask; into the resultant solution was introduced, in small portions with vigorous shaking, crystalline diphenylacetyl chloride in quantity of 2.42 g (0.0105 mole). The last portions of acid chloride dissolved with much difficulty in the reaction mixture and gentle heating was then necessary. After the whole of the acid chloride had been added, the mixture was heated on the boiling water bath for 3 hours, then cooled, diluted with 12-15 ml dry xylene, and the precipitated pyridine hydrochloride filtered off. The filtrate was evaporated in vacuum (to get rid of pyridine) and the residue was again diluted with 7-10 ml dry xylene. The xylene solution was separated from the small precipitate, stood overnight with BaO (for decolorization), and then filtered. The solvent was distilled off in vacuum. The residual diphenylacetate of hydroxyethylmorpholone was a thick, oily liquid with a brownish-orange color. It could not be purified by distillation since it did not distill at 3 mm residual pressure.

For conversion into the diphenylacetate of dihydroxyethylglycine, the unpurified diphenylacetate of hydroxyethylmorpholone was mixed with 5-6 ml water, and the unstable emulsion was heated on the water bath for 5 hours, the volume of heated liquid being kept constant by addition of water to make up for the loss by evaporation. The liquid was later cooled to room temperature and after addition of a seed of crystalline diphenylacetate of dihydroxyethylglycine it was left for a few hours to crystallize. The resultant crystal slurry was diluted with a very small amount of water and transferred to a filter on which it was expressed under vacuum, twice washed with a little ice water and again pressed. The moist cake was dried on filter paper and then transferred to a vacuum desiccator containing calcium chloride in which it was brought to the air-dry state. Yield 3.16 g or 86% of the theoretical. After recrystallization from chloroform-ether the substance melted at 82-84° * and was in the form of long, soft needles (under the microscope), easily soluble in the majority of organic solvents, poorly soluble in water, ether and gasoline.

0.1290 g substance: 0.3174 g CO_2; 0.0768 g H_2O. 0.1105 g substance: 0.2721 g CO_2; 0.0646 g H_2O. 0.4118 g substance: 13.4 ml N_2 (21°, 744 mm). 0.5112 g substance: 16.6 ml N_2 (21°, 739 mm). Found %: C 67.14, 67.20; H 6.66, 6.54; N 3.70, 3.67. $C_{20}H_{23}O_5N$. Calculated %: C 67.21; H 6.49; N 3.92.

N-Hydroxyethylmorpholone diphenylacetate. As stated above, the diphenylacetate of hydroxyethylmorpholone synthesized from hydroxyethylmorpholone and diphenylacetyl chloride could not be purified by distillation. The pure compound was therefore prepared by dehydration of dihydroxyethylglycine diphenylacetate, the reaction proceeding quantitatively and in mild conditions. The weighed amount of the initial ester of dihydroxyethylglycine was placed in a thick-walled test tube which was then connected to a vacuum through a rubber stopper and a leading tube. It was heated at a residual pressure of 10-15 mm on a water bath kept at a temperature of 85-95°. Heating was continued until the test tube and contents had a constant weight; this required 1½ - 2 hours. The diphenylacetate of hydroxyethylglycine was obtained in quantitative yield in the form of a transparent, very viscous liquid with a tinge of yellow, soluble in all the common organic solvents (except saturated hydrocarbons) and sparingly soluble in water. The aqueous solution was neutral to litmus.

0.5141, 0.6755 g dihydroxyethylglycine diphenylacetate: loss in weight after heating in vacuum 0.0251, 0.0338 g. Found loss in weight %: 4.88, 5.00. Calculated loss in weight %: 5.04. Reaction equation: $C_{20}H_{23}O_5N - H_2O = C_{20}H_{21}O_4N$.

Picrolonate of N-hydroxyethylmorpholone diphenylacetate. Prepared by mixing a benzene solution of the diphenylacetate with a solution of picrolonic acid in absolute alcohol. The oil that separated gradually crystallized. The picrolonate forms a yellow crystalline powder with m.p. 135-138°. Soluble in methanol and ethanol. On cooling the alcoholic solutions, it separated as an oil which resisted all attempts at crystallization. It was not subjected to elementary analysis because it could not be obtained pure.

SUMMARY

1. For the first time the acetate, benzoate and diphenylacetate of N-(β-hydroxyethyl)-morpholone-2, their picrates and picrolonates have been synthesized and their properties have been studied.

2. For the first time, by hydrolysis of esters of hydroxyethylmorpholone, the corresponding monoesters of dihydroxyethylglycine have been prepared; these could not be obtained directly from dihydroxyethylglycine and the acid chlorides.

3. On the basis of a comparison of the properties of hydroxyethylmorpholone and its esters, it is suggested that a reciprocal relation exists between the stability and the basicity of morpholone derivatives. The greater the basicity of a morpholone derivative the more easily does opening of the morpholone ring take place and the less easily is it formed.

4. The dibenzoate of dihydroxyethylglycine has been synthesized for the first time.

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* It melts slowly and therefore does not possess a sharp melting point.

** See Consultants Bureau English translation, page 621.

SYNTHESIS AND TRANSFORMATIONS OF SOME DERIVATIVES OF N,N-DI-(β-HYDROXYETHYL)-GLYCINE

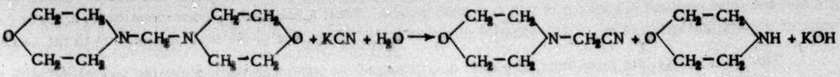
III. SYNTHESIS OF 4-MORPHOLINEACETIC ACID

A. L. Remizov and N. V. Khromov

In our preceding communication [1], it was indicated that the hydrochloride of N,N-di-(β-hydroxyethyl)-glycine undergoes dehydration when heated in vacuum, and that this reaction would be expected to yield two isomeric compounds (in the form of hydrochlorides): N-hydroxyethylmorpholone-2 and 4-morpholine-acetic acid.

Since the hydrochlorides of these two compounds have not been described in the literature and attempts to prepare the salt of the first compound from the free base were unsuccessful, it was proposed to synthesize morpholine-4-acetic acid with the aim of establishing the structure of our product of dehydration of the hydrochloride of dihydroxyethylglycine.

Although neither free morpholineacetic acid nor its hydrochloride, have been described in the literature, a series of other derivatives (including the potassium salt) was already known [2]. The described method of preparation of these compounds is not simple. It is based on the reaction between 4,4'-dimorpholylmethane (product of condensation of morpholine with formaldehyde) and KCN. This reaction gives one molecule of 4-morpholine-acetonitrile and one molecule of morpholine:



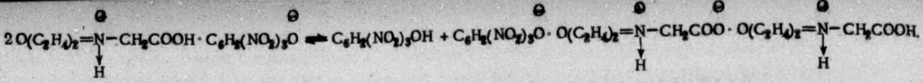
Our own synthesis of 4-morpholine-acetic acid consisted in condensation of morpholine with monochloroacetic acid (as sodium salt) according to the usual reaction.

Morpholine was obtained by dehydrating diethanolamine in concentrated sulfuric acid as described by Medard [3].

The synthesized morpholineacetic acid proved to be so hygroscopic and uncrystallizable that it was impossible to obtain pure. It was transformed into the barium salt and the hydrochloride. Of these salts, only the second possessed adequate stability and crystallizing ability. It was analyzed.

An interesting characteristic of morpholineacetic acid is its ability to form two picrates: one of these is formed from equimolar amounts of components and the other from 1 mole picric acid and two moles morpholineacetic acid. The second picrate (we may call it "semipicrate") is very much more stable than the first, which is appreciably dissociated in solutions to form the "semipicrate" and free picric acid. This mode of dissociation is particularly conspicuous when the normal picrate is dissolved in alcohol; the "semipicrate" is very sparingly soluble in alcohol and comes down from alcoholic solutions of the normal picrate in the form of a precipitate. This dissociation of morpholineacetic acid picrate is reversible and only proceeds up to a certain limit. Hence, the precipitated "semipicrate" can again be transformed into normal picrate by adding a small amount of excess picric acid. This explains why the normal picrate can be prepared in the pure form only by recrystallization in presence of a small amount of excess picric acid.

If we assume that the normal picrate of morpholineacetic acid also functions as a base, then the "semipicrate" may be regarded as a salt of the normal picrate (functioning as an acid) with morpholineacetic acid (functioning as a base). The superior stability of the "semipicrate" and the very fact of its formation indicate that the free carboxyl group of the normal picrate possesses more pronounced acidic properties than the carboxyl group of morpholineacetic acid. Considering the problem from this standpoint, we may reach the conclusion that the normal picrate approaches picric acid in its acidic properties. Actually, on reacting two molecules of the normal picrate, one of them (playing the part of acid) displaces picric acid from the other (acting as salt). In this way we can account for the ability of morpholineacetic acid picrate to dissociate in solutions, as expressed by the scheme:



$$2\,O(C_2H_4)_2{=}\underset{\downarrow\atop H}{\overset{\oplus}{N}}{-}CH_2COOH\cdot C_6H_2(NO_2)_3\overset{\ominus}{O} \rightleftharpoons C_6H_2(NO_2)_3OH + C_6H_2(NO_2)_3\overset{\ominus}{O}\cdot O(C_2H_4)_2{=}\underset{\downarrow\atop H}{\overset{\oplus}{N}}{-}CH_2CO\overset{\ominus}{O}\cdot O(C_2H_4)_2{=}\underset{\downarrow\atop H}{\overset{\oplus}{N}}{-}CH_2COOH.$$

In the course of investigation of the properties of morpholineacetic acid, the dissociation constants were determined by potentiometric titration of its hydrochloride. The apparent acidic ionization constant at 19° was equal to $10^{-7.7}$, the basic constant was $10^{-11.7}$; the corresponding Bjerrum values are $10^{-2.4}$ and $10^{-6.4}$.

EXPERIMENTAL

Barium salt of 4-morpholine-acetic acid. 8.5 g (0.09 g-mole) monochloroacetic acid was dissolved in 10 ml water and carefully neutralized (with cooling) with a solution of 3.6 g (0.09 g-mole) NaOH in 10 ml water. To the solution of sodium monochloroacetate (weakly alkaline to litmus and nearly neutral to Brilliant Yellow paper) was added dropwise, with moderate cooling, 7.85 g (0.09 g-mole) morpholine, after which the reaction mixture was stood at room temperature for 20 minutes and finally heated to the boil to complete the reaction. After boiling for 20 minutes, the medium had acquired a neutral reaction (prior to this it was strongly alkaline to Brilliant Yellow paper). The faint-yellow solution was evaporated on the water bath to a very thick syrup (further evaporation had no effect on the consistency) which was then treated with 75 ml absolute alcohol. The precipitated sodium chloride was filtered off, the filtrate was evaporated in vacuum and the residual gelatinous mass was mixed with a hot solution of 25 g barium hydrate in 70 ml water. The water was distilled off in vacuum, the distillate being collected in a receiver immersed in a freezing mixture. To the dry residue in the distillation flask was added another 80 ml water and the distillation repeated. The same operation was repeated once more. In all, three distillates were collected. They all had an alkaline reaction since they contained the morpholine which had been present in the reaction mass in the form of its salt with glycolic acid formed by the secondary reaction of hydrolysis of monochloroacetic acid. The morpholine content of the three alkaline distillates was determined by titration with acid.

The first distillate required 1.7 ml 2 N HCl or 0.0034 g-mole; the second required 22.0 ml 0.1 N HCl or 0.0022 g-mole; the third required 5.1 ml 0.1 N HCl or 0.0005 g-mole. Total 0.006 g-mole, corresponding to 6.7% or 0.09 g-mole of the original morpholine. Consequently, the reaction had proceeded in the desired direction to the extent of 93%.

The white crystalline mass remaining after distillation of the water and the morpholine was stirred with 150 ml hot water and the excess barium hydrate was precipitated by a current of carbon dioxide (until disappearance of the alkaline reaction to thiazole blue paper). The solution of barium salt of morpholineacetic acid was filtered off from the barium carbonate and evaporated to dryness; the dry residue was treated with a small quantity of boiling absolute alcohol. After filtration from the alcoholic mother liquor, the precipitate was washed on the filter with a little absolute alcohol, then with ether, and dried in a vacuum-desiccator over caustic alkali. Yield 19.1 g. The barium salt was a snow-white crystalline powder, very soluble in water (the aqueous solutions were alkaline to phenolphthalein), methanol and glacial acetic acid, sparingly soluble in ethanol (especially absolute) and almost insoluble in other organic solvents. In the air it rapidly took up carbon dioxide and increased in weight. It could not be purified by crystallization.

4-Morpholine-acetic acid. 14.95 g unpurified barium salt of morpholineacetic acid was dissolved in 50 ml water and the barium quantitatively precipitated as $BaSO_4$ with 2N sulfuric acid (test on filter paper with sodium rhodizonate). The solution was separated from the precipitate by centrifuging and evaporated to dryness first on the water bath and finally in a vacuum-desiccator over sulfuric acid. The slightly moist crystal mass was twice treated with dry acetone and then several times with absolute ether (for removal of glycolic acid). This treatment converted it into a dry crystalline powder. The crystalline morpholineacetic acid prepared in this manner proved to be exceptionally hygroscopic. It was very soluble in methanol, ethanol and glacial acetic acid, much less soluble in acetone, and quite insoluble in ether. It was impossible to purify it and determine its melting point. Yield 8.0 g.

4-Morpholine-acetic acid hydrochloride. 4.0 g crystalline morpholineacetic acid was mixed with 4 ml chemically pure hydrochloric acid (s.g. 1.19) and the mixture evaporated to dryness on the water bath; the resultant crystalline powder was dried in a vacuum-desiccator over solid KOH. Yield quantitative.

After recrystallization from a mixture of absolute alcohol and dry benzene, the compound melted at 169-171° (with frothing); good solubility in methanol, ethanol and glacial acetic acid; poor in acetone, ether and hydrocarbons. Under the microscope it had the form of regular rectangular plates.

0.2429 g substance: 16.7 ml N_2 (27°, 753 mm). 0.2586 g substance: 17.2 ml N_2 (20°, 753 mm). 0.3030 g substance: 0.2386 g AgCl. 0.2210 g substance: 0.1730 g AgCl. Found %: N 7.75, 7.68; Cl 19.48, 19.36. $C_6H_{12}O_3NCl$. Calculated %: N 7.71; Cl 19.53.

4-Morpholine-acetic acid picrate of the composition $O(C_2H_4)_2NCH_2COOH \cdot C_6H_2(NO_2)_3OH$. 0.75 g (0.0052 g-mole) morpholineacetic acid was dissolved in 3 ml absolute alcohol. A solution of 1.17 g picric acid (0.0051 g-mole) in 3 ml benzene was prepared separately. The solutions were mixed. After a short period the crystalline picrate started to come down slowly. The precipitate was filtered, washed on the filter with benzene and ether. Yield 1.52 g or 80% of the theoretical. The substance was recrystallized from alcohol to which a little picric acid had been added. It formed bright-yellow, long hexagonal prisms (under the microscope), very soluble in methanol, ethanol and glacial acetic acid and not quite so soluble in water and acetone. M.p. 141-142°.

Without the addition of picric acid it is impossible to completely dissolve the compound in alcohol because it decomposes with cleavage of free picric acid and is transformed into the other picrate richer in morpholineacetic acid and difficultly soluble in alcohol. The excess picric acid present during the recrystallization of the picrate thus functions as an inhibitor of dissociation of that picrate.

0.2579 g substance: 0.3642 g CO_2; 0.0870 g H_2O. 0.2372 g substance: 0.3352 g CO_2; 0.0804 g H_2O. 0.1198 g substance: 16.2 ml N_2 (26°, 753 mm). 0.1279 g substance: 17.0 ml N_2 (26°, 756 mm). Found %: C 38.54, 38.56; H 3.77, 3.79; N 15.29, 15.19. $C_{12}H_{14}O_{10}N_4$. Calculated %: C 38.50; H 3.77; N 14.97.

4-Morpholine-acetic acid picrate of the composition $[O(C_2H_4)_2NCH_2COOH]_2 \cdot C_6H_2(NO_2)_3OH$. 0.75 g (0.0052 g-mole) morpholineacetic acid was dissolved in the minimum amount of a mixture (1:1) of acetone and glacial acetic acid. A solution of 0.58 g (0.00253 g-mole) picric acid in 3 ml benzene was separately prepared. The solutions were mixed hot. A copious crystalline precipitate came down on cooling and was filtered and washed with alcohol and ether. Yield 1.1 g or 83.5% of the theoretical. After treatment with alcohol followed by recrystallization from a mixture of glacial acetic acid and benzene or absolute alcohol, the compound melted at 170-171°. It formed a pale yellow crystalline powder (slender, long needles under the microscope), readily soluble in glacial acetic acid and sparingly soluble in alcohol.

0.1570 g substance: 0.2414 g CO_2; 0.0708 g H_2O. 0.2280 g substance: 0.3476 g CO_2; 0.1032 g H_2O. 0.1205 g substance: 14.35 ml N_2 (20°, 744 mm). 0.1268 g substance: 15.2 ml N_2 (21°, 739 mm). Found %: C 41.96, 41.61; H 5.05, 5.06; N 13.58, 13.53. $C_{18}H_{25}O_{13}N_5$. Calculated %: C 41.62; H 4.85; N 13.49.

Determination of the ionization constants of 4-morpholine-acetic acid. The acidic and basic constants were determined from the pH values at the half-equivalent points in titration of the hydrochloride of the acid with 0.1 N NaOH solution. The necessary potentiometric measurements were performed with the help of a lamp potentiometer (system GIPKh) with a glass electrode and a saturated calomel half-element as the standard potential electrode.

0.1815 g (0.001 g-mole) morpholineacetic acid was dissolved in 70 ml distilled water; into the solution was run 5.00 ml 0.1 N NaOH. In this way one-half of the hydrochloric acid entering into the composition of the hydrochloride of the amino acid was neutralized, which corresponded to the point of half-equivalence of the amino group. The pH of the solution at this stage was 2.4 at a temperature of 19°. Since the ionic product of water at this temperature is $10^{-14.1}$, then the apparent basic ionization constant of 4-morpholine-acetic acid is $10^{-11.7}$.

For the determination of the pH at the half-equivalent point in respect to the carboxyl group, addition was made to the test solution of a further 10.0 ml 0.1 N NaOH. This brought the pH to 7.7 and, consequently, the apparent acidic ionization constant of 4-morpholine-acetic acid is $10^{-7.7}$ at 19°.

On the basis of the data obtained by the above method, the true ionization constants of morpholineacetic acid were calculated by the usual method (Bjerrum) and found to be $10^{-2.4}$ for the acid constant and $10^{-6.4}$ for the base constant.

SUMMARY

1. Free 4-morpholine-acetic acid and its hydrochloride were synthesized and described for the first time.

2. The constants of electrolytic dissociation of 4-morpholine-acetic acid were determined.

3. It was found that 4-morpholine-acetic acid forms two picrates with different picric acid contents (1 mole and $\frac{1}{2}$ mole picric acid per mole of morpholineacetic acid).

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* GIPKh = State Institute of Applied Chemistry. Publisher.

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* See Consultants Bureau English translation, page 621.

ORGANIC ISOCYANATES

II. TRANSFORMATION OF ISOCYANATES OF THE NAPHTHALENE SERIES BY THE ACTION OF ALUMINUM CHLORIDE

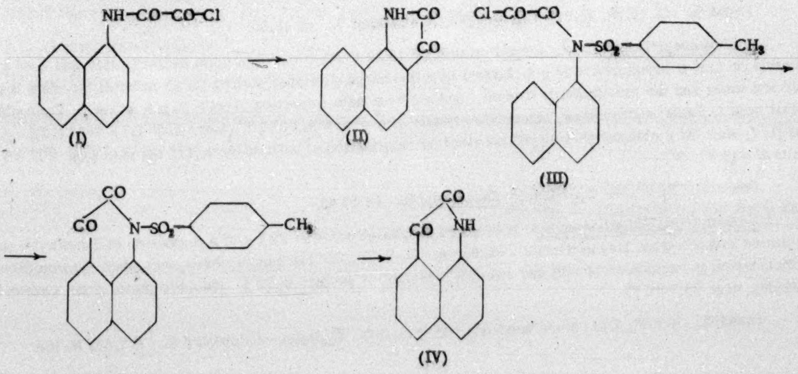
N. S. Dokunikhin and I. D. Pletneva

We previously reported [1] that 1-naphthylisocyanate is converted by fused aluminum chloride into the lactam of 1,8-aminonaphthoic acid (naphthostyril). In view of the fact that isocyanates of the benzene series in these conditions form derivatives of dioxotetrahydroquinazoline [2], from which salts of o-aminocarboxylic acidsmay be obtained by heating with caustic alkali, the entry of the isocyanate group into the 8-position of the naphthalene nucleus is unexpected. These facts make an investigation of the directive influence of the isocyanate group of interest. The latter group may be regarded as an amino group with both the hydrogen atoms substituted by acyl radicals. The literature does not throw any light upon the characteristics of the directive effects of either isocyanates or diacylamino derivatives.

In the majority of cases the introduction of a fresh substituent into diacyl derivatives obtained with participation of monocarboxylic acids gives rise to monoacyl derivatives. Thus, for instance, on nitration of diacetanilide the product is 4-nitro-1-acetanilide [3]. It is difficult to establish whether cleavage of the second acyl residue precedes the introduction of the fresh substituent or whether the monoacylated product is formed in consequence of decomposition of the substituted compound. In this connection more information can be obtained from data relating to cyclic aryl imides of dicarboxylic acids. This grouping remains unchanged during the majority of substitutions of the aromatic nucleus. Thus, for example, by nitration of diacylanilides we obtain p- and o-isomers, just as for monosubstituted derivatives [4]. Nitration of phthaloylnaphthylamines gives up to 60% 1,8-isomer, up to 28% 1,5-isomer and only 5% 1,4-isomer [5].

A similar orientation of substituents is observed with halo derivatives which combine o-, p-orientation with deactivation of the aromatic nucleus, which in the case of naphthalene results in substitution in the second ring.

It is interesting to follow the orienting influence of mono- and diacyl derivatives in two more examples. Fusion of aluminum chloride with 1-naphthyloxamyl chloride gives 1,2-naphthoisatin [7]; in these conditions the N-sulfamido derivative of the same acid chloride is converted into compound (IV) [8].



Formation of naphthostyrils was investigated with reference to 1-naphthylisocyanate, 4-chloro-1-naphthylisocyanate and 2-methyl-1-naphthylisocyanate.

EXPERIMENTAL

1-Naphthylisocyanate was prepared by the action of carbonyl chloride on a suspension of 1-naphthylamine hydrochloride in trichlorobenzene at 170-180°; b.p. 268-270° (269-270° [9]).

Naphthostyril. 3.20 g 1-naphthylisocyanate is introduced into a mixture, heated to 155-160°, of 25.8 g anhydrous aluminum chloride and 6.2 g sodium chloride and stirred for 5 minutes. The reaction mass is poured onto ice water and the precipitate filtered off. One half of the precipitate is heated 3 hours with 50 ml 40% KOH and again filtered. The precipitate is washed free from alkali. The filtrate and the wash liquors are acidified with hydrochloric acid and boiled. A yellow precipitate is formed. Weight 0.45 g, m.p. 176-179°. From ethyl alcohol it forms prisms with m.p. 180.4-181.4°. A mixture with the naphthostyril prepared by alkali fusion of naphthalene-1,8-cyanosulfonate (m.p. 180.6-181.6°) had m.p. 180.4-181.5°.

The second half of the precipitate is repeatedly extracted with boiling 2% sodium carbonate solution. On cooling the soda extract, a yellow crystalline precipitate comes down. Weight 0.47 g, m.p. 177-178°; from ethyl alcohol: prisms with m.p. 180.3-181.3°. A mixture with the naphthostyril prepared by alkali fusion of naphthalene-1,8-cyanosulfonate (m.p. 180.6-181.6°) melts, 180.4-181.5°.

4-Chloro-1-acetylaminonaphthalene is prepared from 1-acetylaminonaphthalene with m.p. 158-159° [10]. The prepared 4-chloro-1-acetylaminonaphthalene has m.p. 186.5-187.0° after one crystallization from aqueous methanol, and 189.5-189.8° after three crystallizations.

4-Chloro-1-naphthylisocyanate. Into 125 ml toluene solution of carbonyl chloride at 0–5° is introduced 40 g 4-chloro-1-naphthylamine with m.p. 95-99°, prepared by saponification of 4-chloro-1-acetylaminonaphthalene with m.p. 186.5-187.0°. The reaction mass is heated to 95°, stirred for 2 hours at this temperature and filtered. The toluene is distilled off from the filtrate and the residue distilled at 1.5 mm and 116.5-117°. Yield 18.78 g of compound; from carbon tetrachloride it forms colorless, lanceolate crystals with m.p. 44.4-45.0°.

The same compound is obtained: 1) by phosgenation of fused 4-chloro-1-acetyl-aminonaphthalene; 2) by phosgenation of a suspension of 4-chloro-1-acetylaminonaphthalene in trichlorobenzene.

Found %: N 6.83, 6.84; M (in benzene) 194.9, 198.3, 194.4. $C_{11}H_6ONCl$. Calculated %: N 6.88; M 203.5.

With methyl alcohol the prepared isocyanate forms a precipitate of methyl-1-naphthylcarbamate; m.p. (from carbon tetrachloride) 149.3-149.7°; colorless prisms. A mixture with the compound prepared from 4-chloro-1-naphthylamine and methyl chloroformate (m.p. 149.6-149.9°), melts at 149.6-149.8°.

Found %: Cl 14.98, 15.01. $C_{12}H_{10}O_2NCl$. Calculated %: Cl 15.05.

4-Chloronaphthostyril. Into a fused mixture of 24.20 g anhydrous aluminum hydrochloride and 5.80 g sodium chloride at 115° is introduced 2.95 g 4-chloro-1-naphthylisocyanate; after stirring for 15 minutes the mass is poured onto ice water and the precipitate is filtered. Sodium carbonate extraction gives 0.92 g substance. From glacial acetic acid it forms bright-yellow, lanceolate crystals with m.p. 274.1-274.7° (about 267° [11]; 270° [12]). A mixed test (1:1) with the 4-chloronaphthylstyril prepared by chlorination of naphthostyril [11, 13] with m.p. 273.3-273.7°, melts at 273-274.3°.

Found %: Cl 17.37. $C_{11}H_6ONCl$. Calculated %: Cl 17.43.

2-Methyl-1-naphthylisocyanate is prepared by phosgenation of 59.7 g of a suspension of 2-methyl-1-naphthylamine hydrochloride [14] in trichlorobenzene at 160-170°. The isocyanate comes over when the reaction mass is fractionated in vacuum at 14 mm and 161-162°. Weight of product 33.22 g. Rhombic plates (from carbon tetrachloride), m.p. 28.7-29.3°.

Found %: N 7.56, 7.44; M (in benzene) 173, 175, 174. $C_{12}H_9ON$. Calculated %: N 7.65; M 183.

With methyl alcohol the compound forms a white precipitate of methyl 2-methyl-1-naphthylcarbamate; from methyl alcohol it crystallizes in prisms with m.p. 148.7-149.5°. The mixture with the substance prepared from 2-methyl-1-naphthylamine and methyl chloroformate, m.p. 147.5-148.2°, melts at 147.5-148.7°.

Found %: N 6.75, 6.73. $C_{13}H_{13}O_2N$. Calculated %: N 6.51.

2-Methylnaphthostyril. Into a fused mixture of 24.20 g anhydrous aluminum chloride and 5.80 g sodium chloride at 115° is introduced 2.98 g 2-methyl-1-naphthylisocyanate. The mixture is stirred 15 minutes and poured onto ice water. The precipitate is filtered, extracted with boiling 2% sodium carbonate. On cooling, the extract deposits yellow crystals. Weight 0.47 g. From ethyl alcohol it crystallizes as yellow prisms, m.p. 213.9-214.1°.

Found %: N 7.62, 7.61; M (in camphor) 215.7. $C_{12}H_9ON$. Calculated %: N 7.65; M 183.

SUMMARY

1. Reaction of 1-naphthylisocyanate and its derivatives with fused aluminum chloride is found to give 8-amino-1-naphthoic lactam (naphthostyril) and its derivatives. The reaction was followed with 1-naphthylisocyanate, 4-chloro-1-naphthylisocyanate, and 2-methyl-1-naphthylisocyanate.

2. The hypothesis is advanced that the isocyanate and diacylamino groups may be classed with halogens in respect to their orienting effect on introduction of a fresh substituent into the aromatic nucleus, since they combine para-, ortho- orientation with deactivation of the aromatic nucleus.

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*See Consultants Bureau English Translation, p. 629 ff.

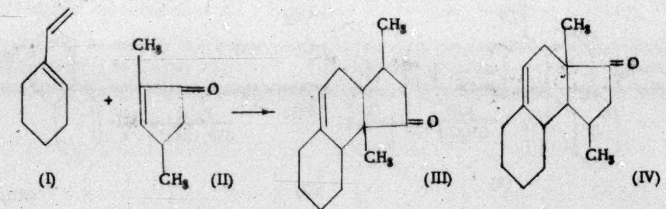
ACETYLENE DERIVATIVES, 154.

POLYCYCLIC HYDROCARBONS RELATED TO THE STEROIDS

XXVI. STRUCTURE OF THE TRICYCLIC KETONES PREPARED BY THE DIENE CONDENSATION OF 1-VINYL-Δ^1-CYCLOHEXENE WITH 1,3-DIMETHYL-Δ^1-CYCLOPENTEN-5-ONE

I. N. Nazarov and T. D. Nagibina

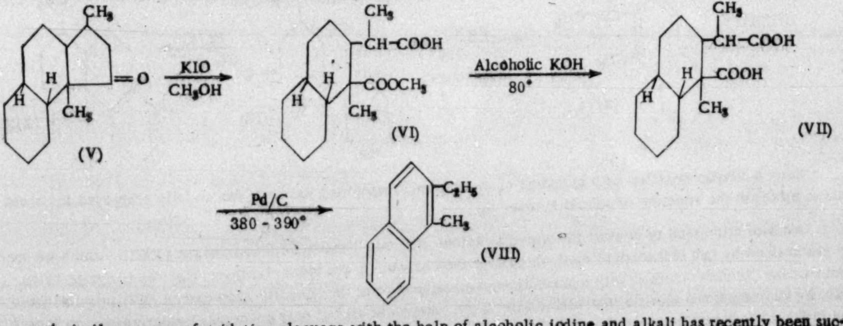
In one of the preceding investigations [1], it was shown that the diene condensation of 1-vinyl-Δ^1-cyclohexene (I) with 1,3-dimethyl-Δ^1-cyclopenten-5-one (II) gives two isomeric tricyclic ketones (a crystalline one with m.p. 61-62° and a liquid one with b.p. 147° at 7 mm), whose structure was represented by the formulas (III) and (IV):



The amount of liquid isomer increased with rising temperature of the diene condensation; however, the crystalline isomer is not transformed into the liquid one even when heated in a glass ampoule at 200-210° for 20 hours.

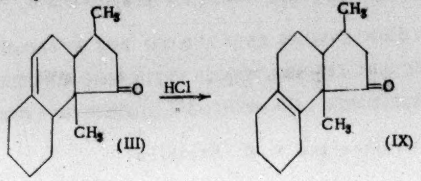
In view of the fact that great interest attaches to the described diene condensation as the simplest model example for the synthesis of polycyclic compounds related to the steroids, we decided to undertake a direct demonstration of the structure of the tricyclic ketones that we obtained by this condensation. Another reason for doing this was the fact that little attention has hitherto been given to diene condensations of 1,2-substituted butadienes with asymmetrical dienophiles, although these condensations are of great theoretical and synthetic value.

Detailed investigations revealed that the crystalline isomer with m.p. 61-62° was 1,9-dimethyl-4,5-tetramethylene-Δ^5-hydrindane-3-one (III), whose structure was proved by hydrogenation to the saturated tricyclic ketone (V) and by oxidation of the ketone with iodine and alkali in methanol solution to the polyester of the dicarboxylic acid (VII); the latter was dehydrogenated and decarboxylated in presence of palladium-on-carbon at 380-390° to the known 1-methyl-2-ethylnaphthalene (VIII) [2].

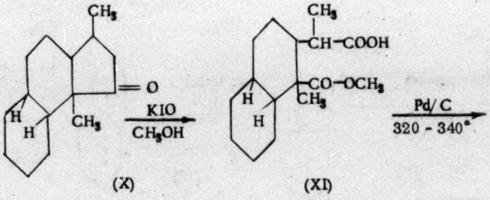


A similar process of oxidative cleavage with the help of alcoholic iodine and alkali has recently been successfully employed to demonstrate the structure of some steroid ketones [3].

The liquid tricyclic ketone (b.p. 147° at 7 mm) proved to be 1,9-dimethyl-4,5-tetramethylene-Δ^4-hydrindane-3-one (IX), which was formed by diene condensation from the crystalline isomer (III) with double bond migration. This isomerization of the crystalline ketone (III) into the liquid isomer (IX) is realized with exceptional ease by heating with hydrochloric acid, as was repeatedly described previously in other cases [4]:



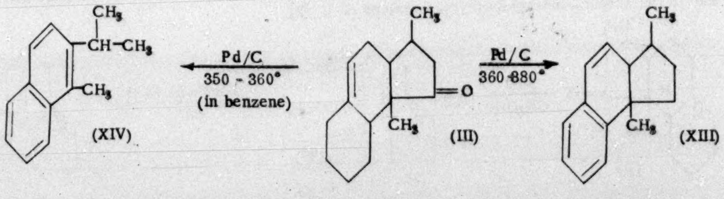
The structure of the liquid tricyclic ketone (IX) was also proved by hydrogenation to the saturated tricyclic ketone (X), oxidation of which with iodine and alkali in methanol solution gave the polyester (XI) which was dehydrogenated to 2-ethylnaphthalene (XII):



2-Ethylnaphthalene (XII) was also prepared by dehydrogenation of the above-described dicarboxylic acid (VII) with Ni catalyst (25 hours at 380-390°). It must be pointed out that hydrogenation with Pt catalyst of the tricyclic ketones (III) and (IX) leads to formation of different stereoisomeric ketones (V) and (X), differing in all probability by the configuration of the carbons at the place of addition of the first and second rings.

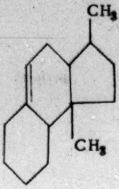
Consequently, in the diene condensation of 1-vinyl-Δ^1-cyclohexene (I) with 1,3-dimethyl-Δ^1-cyclopentene-5-one (II), only ketones (III) and (IX), which possess an identical skeleton and differ only in the position of the double bond, are formed. The ketone (IV), suggested above, is apparently not formed at all.

The tricyclic hydrocarbon (XIII) is formed on dehydrogenation of the crystalline ketone (III) with the help of palladium-on-carbon (5% Pd) at 360-380°. On carrying out this dehydrogenation in benzene solution, cleavage of the 5-membered ring occurs with formation of a hydrocarbon $C_{14}H_{16}$ which, in all probability, is 1-methyl-2-isopropylnaphthalene (XIV):

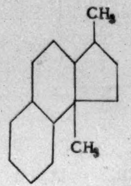


Such a dehydrogenation with cleavage of the five-membered ring has been successfully employed in recent years to establish the structure of steroid ketones [5].

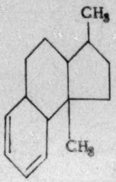
We also attempted to convert the tricyclic ketone (III) into 1-methyl-4,5-benzindane (XXIII), which we specially synthesized by two independent methods as described below. It was found, however, that the tricyclic ketone (III) is reduced by Kizhner's method with extraordinary difficulty to form the tricyclic hydrocarbon (XV) in small yield, while, by Clemmensen's method, the ketone (III) is not reduced at all but only undergoes isomerization, with double-bond shift, to the liquid ketone (IX). In this connection, it must be pointed out that Clemmensen's reduction fails to occur with all other bi-, tri- and polycyclic ketones containing the 1,9-dimethyl hydrindane-3-one grouping [6]. The corresponding bi-, tri- and polycyclic hydrocarbons containing the 1,9-dimethylhydrindane grouping are extraordinarily resistant to exhaustive dehydrogenation with elimination of the angular methyl group [6]:



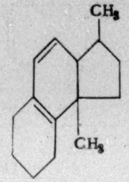
(XV)



(XVI)



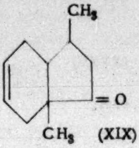
(XVII)



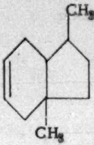
(XVIII)

By Kizhner's reduction of the saturated tricyclic ketone (V), it was possible to obtain in satisfactory yield (about 40%) the saturated tricyclic hydrocarbon (XVI) which, however, was not susceptible to exhaustive dehydrogenation to 1-methyl-4,5-benzindane (XXIII); even in very drastic conditions of dehydrogenation it only loses two molecules of hydrogen and is converted into a hydrocarbon with either structure (XVII) or (XVIII).

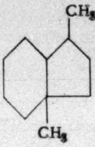
A similar striking stability in dehydrogenation conditions was also exhibited by the 1,9-dimethylhydrindanes (XX) and (XXI), prepared by Kizhner reduction of 1,9-dimethyl-Δ^6-hydrindane-3-one (XIX); this compound was synthesized in our laboratory previously by condensation of 1,3-dimethyl-Δ'-cyclopenten -5-one (I) with butadiene [7]:



(XIX)

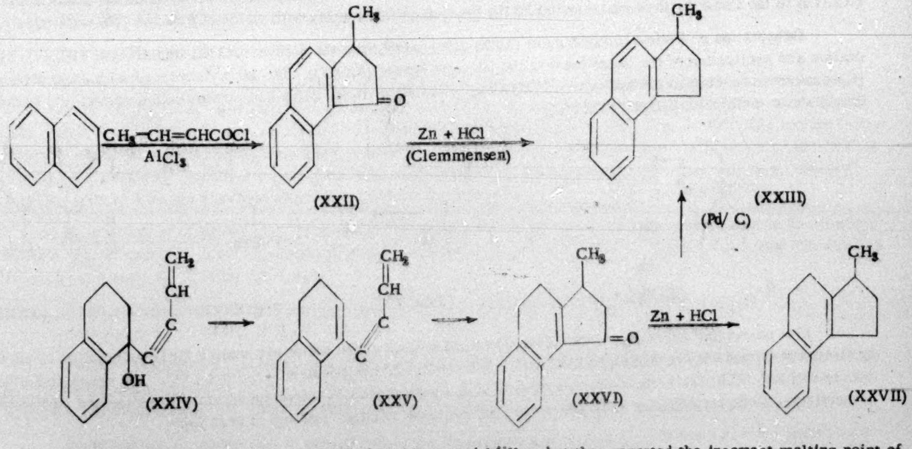


(XX)

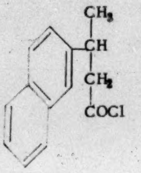


(XXI)

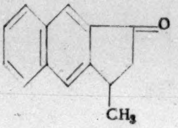
1-Methyl-4,5-benzindane (XXIII), constituting the basis of the tricyclic ketones (III) and (IX), was synthesized by us by the two following independent routes:



Ketone (XXII) has already been described by Mayor and Müller, but they reported the incorrect melting point of 99° (instead of 71-72°) on the basis of which Banchetti [8] apparently erroneously ascribed to the product of cyclization of β-(2-naphthyl)-butyryl chloride (XXVIII) the structure of the linear ketone (XXIX) although it had the same melting point as ketone (XXII):

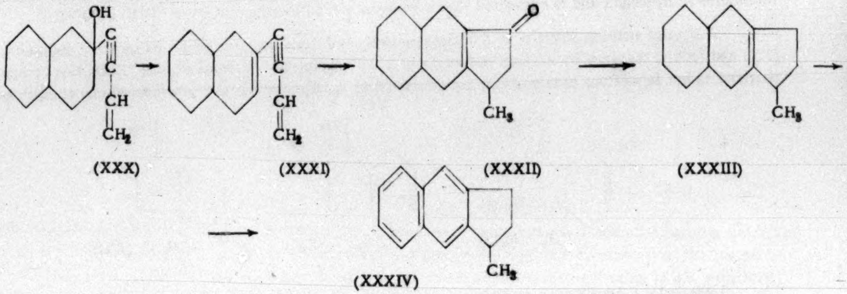


(XXVIII)



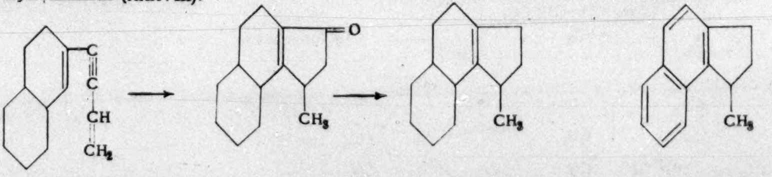
(XXIX)

Clemmensen reduction of ketones (XXII) and (XXVI) proceeds smoothly and 60-70% yields are obtained of the corresponding hydrocarbons (XXIII) and (XXVII); the latter also gives hydrocarbon (XXIII) on dehydrogenation with palladium-on-carbon. Starting from the cis- and trans-β-vinylethinyldecalols (XXX), we also prepared the linear methylbenzindane (XXXIV) by the following route which was developed in our laboratory [9]:



Reduction of ketone (XXXII) by the Clemmenson method and dehydrogenation of the resultant hydrocarbon (XXXIII) to the linear methylbenzindane (XXXIV) proceed quite smoothly with yields of 80% and 60% respectively.

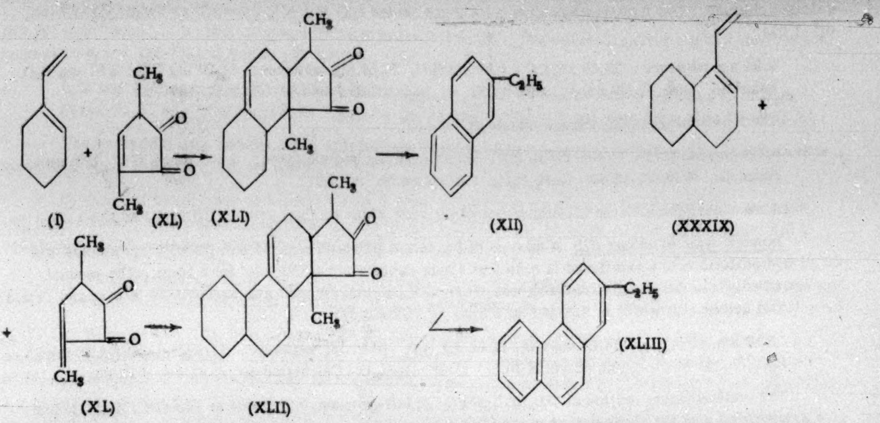
Dehydration of β-vinylethinyldecalol (XXX) gives, apart from the dienyne (XXXI), the dienyne (XXXV); hydration and cyclization of the latter leads to the tricyclic ketone (XXXVI). The latter is reduced with great difficulty (Clemmensen reaction) to the hydrocarbon (XXXVII) (yield about 15%), which had already failed completely to dehydrogenate to methylbenzindane (XXXVIII):



Also proceeding according to the above-described scheme is the previously studied [10] condensation of vinylcyclohexene (I) and vinyloctaline (XXXIX) with 1,3-di-methyl-Δ^1-cyclopenten -4,5-dione (XL). The crystalline diketones (XLI) and (XLII) are formed, the structures of which were proved by dehydrogenation with palladized carbon to, respectively, 2-ethylnaphthalene (XII) and 2-ethylphenanthrene (XLIII): (see top of next page)

EXPERIMENTAL

Condensation of 1-vinyl-Δ^1-cyclohexene (I) with 1,3-dimethyl-Δ^1-cyclopenten-5-one (II). a) 18 g 1-vinyl-Δ^1-cyclohexene (b.p. 142-144°; n_D^{20} 1.4900) and 45 g 1,3-dimethyl-Δ^1-cyclopenten-5-one (b.p. 164-165°; n_D^{20} 1.4660) were



heated in a sealed ampoule at 125-130° for 60 hours. After distilling off the original substances, the residue was fractionated in vacuum to give 10 g of a mixture of ketones (III) and (IX) with b.p. 125-128° at 3 mm; n_D^{20} 1.5150. Repeated freezing with addition of methyl alcohol led to isolation of 8 g crystalline ketone (III) with m.p. 61-62° (from methyl alcohol); it gives a dinitrophenylhydrazone with m.p. 165-166° (from alcohol).

5.105 mg substance: 0.627 ml N_2 (23°, 752 mm). 5.310 mg substance: 0.642 ml N_2 (23° 752 mm). Found %: N 14.00, 13.80. $C_{21}H_{26}N_4O_4$. Calculated %: N 14.07.

Ketone (III) does not form a semicarbazone even after boiling of the reactants for many hours. Ketone (III) is only hydrogenated with Pt catalyst in anhydrous acetic acid or in ethyl alcohol, but with addition in the latter case of Pd catalyst on calcium carbonate. In this process one molecule of hydrogen combines to form the saturated ketone (V) with m.p. 37-38° (from alcohol). Its 2,4-dinitrophenylhydrazone melts at 158-159° (from alcohol).

4.770 mg substance: 0.571 ml N_2 (19°, 749 mm). 4.685 mg substance: 0.563 ml N_2 (20°, 748 mm). Found %: N 13.79, 13.78. $C_{21}H_{28}N_4O_4$. Calculated %: N 14.00.

Ketone (V) likewise fails to form a semicarbazone.

b) 19 g 1-vinyl-Δ°-cyclohexene and 50 g 1,3-dimethyl-Δ'-cyclopenten-5-one were heated in a sealed ampoule at 170° for 50 hours. Distillation of the original substances was followed by isolation of 12 g ketones (III) and (IX) with b.p. 137-144° at 4 mm; n_D^{18} 1.5180. Freezing yielded 7 g ketone (III) with m.p. 61-62°. The mother liquor from two experiments was combined and fractionated in vacuum to give 7 g liquid ketone (IX) with b.p. 125-127° at 4 mm; n_D^{22} 1.5175; d_4^{20} 1.018; semicarbazone with m.p. 186-187°; 2,4-dinitrophenylhydrazone with m.p. 166-167°. A mixed sample with the above-described 2,4-dinitrophenylhydrazone of ketone (III) melts at 144-150°.

Hydrogenation of ketone (IX). 6 g ketone (IX) with b.p. 125-127° at 4 mm was hydrogenated in 25 ml ethyl alcohol over Pt catalyst. 0.62 l. hydrogen (1 mole) combined in a period of 2 hours. Yield 5.8 g ketone (X) with b.p. 127-129° at 4 mm; n_D^{20} 1.5098; d_4^{20} 1.010.

5.080 mg substance: 15.302 mg CO_2; 4.865 mg H_2O. Found %: C 82.20; H 10.71. $C_{15}H_{24}O$. Calculated %: C 81.81; H 10.90.

Ketone (X) gives a 2,4-dinitrophenylhydrazone with m.p. 157-158°; a mixed sample with the above-described 2,4-dinitrophenylhydrazone of ketone (V) melts at 135-142°, i.e., a strong depression occurred. The semicarbazone of ketone (X) melts at 193-194° (from alcohol).

Isomerization of ketone (III) in the conditions of the Clemmensen reaction. A mixture of 7.8 g ketone (III) (m.p. 61-62°), 30 ml ethyl alcohol, 25 g amalgamated zinc, 20 ml water and 50 ml hydrochloric acid was boiled under a reflux condenser for 7 hours. Bath temperature 120-130°. During this period a further 60 ml hydrochloric acid was added in three portions. The product was extracted with ether, neutralized with soda, and dried with calcium chloride. Two fractionations gave 5.1 g liquid ketone (IX) with b.p. 133-135° at 6 mm; n_D^{20} 1.5185; d_4^{20} 1.024.

9.94 mg substance: 30.00 mg CO_2; 9.33 mg H_2O. 10.58 mg substance: 31.90 mg CO_2; 9.81 mg H_2O. Found %: C 82.37, 82.28; H 10.51, 10.38. $C_{15}H_{22}O$. Calculated %: C 82.57; H 10.04.

The 2,4-dinitrophenylhydrazone melted at 165-167°.

5.588 mg substance: 0.666 ml N_2 (22°, 752 mm). 5.450 mg substance: 0.647 ml N_2 (21°, 753 mm). Found %: N 13.65, 13.66. $C_{21}H_{26}N_4O_4$. Calculated %: N 14.07.

A mixed sample with the 2,4-dinitrophenylhydrazone of the original ketone (III) melts at 128-130°.

Isomerization of ketone (III). A mixture of 5 g ketone (III) with m.p. 61-62°, 20 ml ethyl alcohol and 50 ml hydrochloric acid was refluxed in a flask at a bath temperature of 125-130° for 5 hours. The product was extracted with ether, neutralized with soda, dried with calcium chloride and fractionated in vacuum. Yield 3.5 g liquid ketone (IX) with b.p. 139-140° at 8 mm; n_D^{20} 1.5185; d_4^{20} 1.021.

12.23 mg substance: 36.76 mg CO_2; 11.32 mg H_2O. 10.51 mg substance: 31.69 mg CO_2; 9.78 mg H_2O. Found %: C 82.03, 82.28; H 10.35, 10.42. $C_{15}H_{22}O$. Calculated %: C 82.57; H 10.04.

The semicarbazone melted at 186-187°, and the 2,4-dinitrophenylhydrazone at 163-164°; they did not give a depression with the above-described semicarbazone and 2,4-dinitrophenylhydrazone of liquid ketone (IX) prepared by diene condensation of 1-vinyl-Δ'-cyclohexene with 1,3-dimethyl-Δ'-cyclopenten-5-one.

Reduction of ketone (III). 5 g ketone (III) with m.p. 61-62°, 40 g diethylene glycol, 20 ml ethyl alcohol and 11 ml hydrazine hydrate were refluxed on a water bath for 3 hours; 4 g KOH was then added and the heating continued with a sloping condenser for 12 hours at 200-210°. 15 ml turbid liquid distilled over. The residue was diluted with water and extracted with ether; the distillate was also extracted with ether; the ethereal solutions were combined and dried with calcium chloride. Fractionation gave: 1) a fraction with b.p. 110-150° at 6 mm; n_D^{20} 1.5140, 1 g; 2) a fraction with b.p. 160-164° at 6 mm; n_D^{20} 1.5330, 3 g.

The first and second fractions were further heated with 1 g fused KOH at 280° for 8 hours to give 0.5 g hydrocarbon (XV) with b.p. 112-114° at 7 mm; n_D^{22} 1.5140.

Reduction of ketone (V). 4.2 g ketone (V) with m.p. 36-37°, 20 ml ethyl alcohol, 40 ml diethylene glycol and 11 ml hydrazine hydrate were heated on a boiling water bath for 3 hours. Heating was then continued for 2 hours at 170-190° and 7 hours at 210-215°. The product was diluted with water, extracted with ether and dried with calcium chloride. After distilling off the ether, the residue did not distill at 7 mm and a bath temperature of 170°. 2 g fused KOH was added to it and the mixture heated at 310-320°. Vigorous evolution of nitrogen was observed and a hydrocarbon distilled over. The hydrocarbon was extracted with ether and dried with calcium chloride. Fractionation gave 1.6 g hydrocarbon (XVI) with b.p. 118-119° at 9 mm; n_D^{20} 1.5090; d_4^{20} 0.9616; MR_D 64.00; calculated 64 87.

12.37 mg substance: 39.50 mg CO_2; 13.52 mg H_2O. 12.65 mg substance: 40.33 mg CO_2; 13.98 mg H_2O. Found %: C 87.15, 87.11. H 12.23, 12.37. $C_{15}H_{26}$. Calculated %: C 87.37; H 12.63.

Dehydrogenation of hydrocarbon (XVI). a) 1.4 g hydrocarbon (XVI) (b.p. 118-119° at 9 mm; n_D^{20} 1.5090). 1.5 g palladium on carbon (5% Pd) and 15 ml benzene were heated at 360-370° for 10 hours in a metal ampoule. Fractionation gave 1 g of a mixture of products with b.p. 115-117° at 7 mm; n_D^{20} 1.5140. Judging by the refractive index, very little hydrogenation had taken place in this experiment.

b) 0.7 g hydrocarbon (XVI) from the preceding experiment with b.p. 115-117° at 7 mm was heated with 0.5 g selenium at 420° in a flask with a reflux condenser; evolution of hydrogen selenide was not observed. At a temperature of 435° a little hydrogen selenide came off and the mixture was badly resinified.

c) 1.5 g hydrocarbon (XVI) (b.p. 118-119° at 9 mm; n_D^{20} 1.5090) was passed at 360-370° for two hours through a tube packed with palladium on carbon (5% Pd). 340 ml hydrogen came off (2 moles). Fractionation gave 0.7 g hydrocarbon (XVII) or (XVIII) with b.p. 142-145° at 8 mm; n_D^{22} 1.5340.

5.147 mg substance: 16.73 mg CO_2; 4.935 mg H_2O. 8.300 mg substance: 26.930 mg CO_2; 8.023 mg H_2O. Found %: C 88.71, 88.54; H 10.73, 10.82. $C_{15}H_{22}$. Calculated %: C 89.11; H 10.89.

Dehydrogenation of ketone (III). a) 4 g ketone (III) with m.p. 61-62° and 4 g palladium-on-carbon (5% Pd) were heated in a metal ampoule for 15 minutes at 360-380°. Fractionation gave 2.5 g of a mixture of ketones with b.p. 130-132° at 3 mm; n_D^{23} 1.5310.

9.98 mg substance: 30.85 mg CO_2; 8.77 mg H_2O. 14.78 mg substance: 46.03 mg CO_2; 12.90 H_2O. Found %: C 85.21, 84.99; H 9.93, 9.77. For the original ketone (III) calculated %: C 82.57; H 10.04.

The analytical data and the index of refraction show that dehydrogenation of ketone (III) in this experiment took place to an insignificant extent.

b) 2.5 g of the mixture of ketones with b.p. 130-132° at 3 mm obtained in the preceding experiment was further heated with 2 g palladium-on-carbon (5% Pd) at 360-380° for $1\frac{1}{2}$ hours. There was obtained 0.8 g hydrocarbon (XIII) with b.p. 130-134° at 4 mm; n_D^{20} 1.5780.

9.76 mg substance: 32.48 mg CO_2; 7.83 mg H_2O. 11.17 mg substance: 37.11 mg CO_2; 9.15 mg H_2O. Found %: C 90.82, 90.67; H 8.97, 9.17. $C_{15}H_{18}$. Calculated %: C 90.91; H 9.09.

c) 2.5 g ketone (III), 25 g benzene and 2 g palladium-on-carbon (5% Pd) were heated in a metal ampoule at 350-360° for 6 hours. The catalyst was filtered off and repeatedly washed with benzene. After distilling off the benzene, the product was fractionated in vacuum; first fraction b.p. 110-123° at 7 mm; n_D^{20} 1.5781, 0.5 g; second fraction b.p. 123-124° at 7 mm; n_D^{20} 1.5780, 1.25 g.

The first and second fractions were further dehydrogenated with 1 g palladium-on-carbon (5% Pd) at 350-380° for 6 hours to give 1 g fraction with b.p. 126-169° at 6 mm; n_D^{19} 1.5910. This product was again dehydrogenated with 1 g palladium on carbon (5% Pd) at 360-380° for 4 hours to give 0.6 g 1-methyl-2-isopropylnaphthalene (XIV) with b.p. 127-129° at 5 mm; n_D^{20} 1.5970; d_4^{20} 1.0137.

7.716 mg substance: 25.713 mg CO_2; 5.772 mg H_2O. Found %: C 90.94; H 8.37. $C_{14}H_{16}$. Calculated %: C 91.30; H 8.70.

The picrate melted at 99-100° (from alcohol).

4.172 mg substance: 0.381 ml N_2 (23°, 739 mm). 2.451 mg substance: 0.220 ml N_2 (24°, 752 mm). Found %: N 10.24, 10.21. $C_{20}H_{19}O_7N_3$. Calculated %: N 10.16.

Oxidative cleavage of ketone (V). To 8 g ketone (V) with m.p. 37-38° and 500 ml methyl alcohol were simultaneously added, dropwise over a period of 3 hours, solutions of 32 g iodine in 480 ml methyl alcohol and 22.8 g KOH in 400 ml methyl alcohol and 80 ml water at such a rate that the iodine was in excess. On the next day the methyl alcohol was distilled off in a moderate vacuum and the residue extracted with ether for removal of the neutral products. The residue from the extraction was treated with hydrochloric acid, the acid products were extracted with ether; the ethereal solution was decolorized by shaking with concentrated sodium bisulfite solution and dried with sodium sulfate. Distillation of the ether left 6 g half-ester (VI) with m.p. 111-112° (from ligroine).

9.98 mg substance: 25.15 mg CO_2; 8.47 mg H_2O. Found %: C 68.77; H 9.48. $C_{16}H_{26}O_4$. Calculated %: C 68.08; H 9.21.

From the neutral fraction, after distillation of the ether, was isolated 0.6 g crystalline substance with m.p. 79-81° (from alcohol) whose structure was not established.

3.565 mg substance: 9.574 mg CO_2; 3.070 mg H_2O. 3.924 mg substance: 10.554 mg CO_2; 3.304 mg H_2O. Found %: C 73.29, 73.37; H 9.63, 9.42.

Saponification of the half-ester (VI). 5 g half-ester (VI) was heated with 100 ml 10% alcoholic KOH solution for 6 hours. After distilling off the alcohol, the residue was extracted with ether to remove neutral products but there was hardly a trace of these. The residue was acidified with hydrochloric acid (20 ml) and extracted with ether. From the ethereal solution was obtained 2.5 g dicarboxylic acid (VII) with m.p. 167-169° (from acetone).

9.70 mg substance: 23.84 mg CO_2; 7.80 mg H_2O. 10.28 mg substance: 25.25 mg CO_2; 8.47 mg H_2O. 0.12 g substance: 8.85 ml 0.1 N KOH. Found %: C 67.07, 67.03; H 9.09, 9.27; M 270. $C_{15}H_{24}O_4$. Calculated %: C 67.16; H 8.98; M 268.

Dehydrogenation of acid (VII). a) 1.5 g acid (VII), 10 ml benzene and 1.5 g palladium-on-carbon (5% Pd) were heated in a metal ampoule for 7 hours at 380-390°. At the end of the reaction, the catalyst was filtered off and washed several times with benzene. The benzene was distilled off. Distillation of the residue in vacuum gave 0.5 g hydrocarbon fraction with b.p. 125-132° at 15 mm; n_D^{20} 1.5620; this gave the picrate of 1-methyl-2-ethylnaphthalene with m.p. 94-95°.

3.651 mg substance: 0.331 ml N_2 (19°, 745 mm). 5.080 mg substance: 0.461 ml N_2 (22°, 751 mm). Found %: N 10.39, 10.35. $C_{19}H_{17}O_7N_3$. Calculated %: N 10.52.

According to the literature [2], 1-methyl-2-ethylnaphthalene picrate melts at 110-111°.

b) 1.5 g acid (VII), 100 ml benzene and 3 g Raney nickel were heated at 380-390° for 25 hours. The benzene was distilled off and the residue fractionated in vacuum to give 0.3 g 2-ethylnaphthalene (XII) with b.p. 140-142° at 15 mm; n_D^{20} 1.5610; the picrate melted at 78-80°.

Oxidative cleavage of ketone (X). To 4 g ketone (X) (b.p. 127-129° at 4 mm) in 300 ml methyl alcohol were simultaneously added, over a period of 4 hours, solutions of 16 g iodine in 200 ml methyl alcohol and 11.4 g KOH in 200 ml methyl alcohol and 40 ml mater at such a speed that the iodine was in excess. The next day the methyl alcohol was distilled off in vacuum, the residue was worked up with hydrochloric acid and the acid products were extracted with ether. The ethereal solution was decolorized by shaking with 5 ml concentrated sodium bisulfite solution and dried with sodium sulfate. The ether was distilled off and the product distilled in vacuum to give 5.1 g noncrystallizing half-ester (XI) which was not saponified when heated with 10% alcoholic KOH solution.

0.2268 g substance: 8.09 ml 0.1 N KOH. Found: M 280. $C_{16}H_{26}O_4$. Calculated: M 282.

Dehydrogenation of the half-ester (XI). 2.9 g half-ester (XI), 15 ml benzene and 2 g palladium-on-carbon (5% Pd), were heated at 320-340° for 5 hours. The ampoule was opened, the hydrogen released and the heating continued at 360° for 11 hours. The catalyst was filtered off, washed with benzene; the benzene was distilled off and the residue fractionated in vacuum. Yield 0.7 g of fraction with b.p. 115-120° at 5 mm; n_D^{25} 1.5630; from this was prepared the picrate of 2-ethylnaphthalene (XII) with m.p. 78-80° (from alcohol).

3.521 mg substance: 0.319 ml N_2 (22°, 752 mm). 2.351 ml substance: 0.216 ml N_2 (24°, 758 mm). Found %: N 10.38, 10.53. $C_{18}H_{15}O_7N_3$. Calculated %: N 10.90.

According to the literature [11], 2-ethylnaphthalenepicrate melts at 76-77°, and 1-ethylnaphthalene picrate melts at 98.5°.

1-Methyl-4,5-benzindane-3-one (XXII). 12.8 g naphthalene and 10.4 g crotonic anhydride (m.p. 112-114°; n_D^{20} 1.4590) were simultaneously added with energetic stirring to 30 g aluminum chloride in 100 ml carbon bisulfide. When all had been added, the mixture was stirred for 4 hours at room temperature and treated with 15% soda solution. The carbon bisulfide layer was separated and dried with calcium chloride; the residue, after distillation of the carbon bisulfide, was fractionated in vacuum to give 6.3 g ketone (XXII) with b.p. 202-204° at 15 mm and m.p. 71-72° (from carbon tetrachloride).

5.868 mg substance: 3.308 mg CO_2; 18.495 mg H_2O. 3.760 mg substance: 2.220 mg CO_2; 11.834 mg H_2O. Found %: C 85.98, 85.85; H 6.35, 6.60. $C_{14}H_{12}O$. Calculated %: C 85.71; H 6.12.

A semicarbazone could not be prepared.

1-Methyl-4,5-benzindane (XXIII). a) 4.6 g of the above ketone (XXII) with m.p. 71-72°, 35 ml ethyl alcohol, 15 g amalgamated zinc, 20 ml water and 50 ml hydrochloric acid were heated at 130° for 7 hours. The mixture was diluted with water, saturated with potassium carbonate and extracted with ether; the ethereal solution was dried with calcium chloride. Fractionation gave 3 g hydrocarbon (XXIII) with b.p. 133-134° / 6 mm; n_D^{20} 1.6132; d_4^{20} 1.0413.

9.93 mg substance: 33.47 mg CO_2; 6.88 mg H_2O. 9.08 mg substance: 30.64 mg CO_2; 6.24 mg H_2O. Found %: C 91.99, 92.09; H 7.73, 7.69. $C_{14}H_{14}$. Calculated %: C 92.30; H 7.70.

The picrate melted at 88-89° (from alcohol).

5.070 mg substance: 0.462 ml N_2 (19°, 745 mm). 5.340 mg substance: 0.477 ml N_2 (19°, 745 mm). Found %: N 10.44, 10.24. $C_{20}H_{17}O_7N_3$. Calculated %: N 10.21.

b) To an ethereal solution of vinylacetylene magnesium bromide prepared from 8.2 g magnesium, 41 g ethyl bromide, 25 g vinylacetylene in 320 ml ether at room temperature was added, over a period of 1$\frac{1}{2}$ hours, 36 g α-tetralone (b.p. 118-120° at 10 mm, n_D^{20} 1.5698) in 200 ml ether. After the whole of the ketone had been added, the mixture (pink color) was stirred for 3 hours. The next day 40 ml water and 150 ml 10% hydrochloric acid were stirred in. The ethereal solution was separated, neutralized with soda solution, washed with water and dried with magnesium sulfate. Fractionation of the reaction products in a nitrogen stream was accompanied by cleavage of water, and 17 g of a mixture of the carbinol (XXIV) and the hydrocarbon (XXV) was obtained with b.p. 126-134° at 4 mm; n_D^{18} 1.6180 [12]. The substance was heated with a mixture of 3.5 ml sulfuric acid, 10 g mercuric sulfate and 180 ml 95% methyl alcohol at 60° for 18 hours. The alcohol was distilled off in vacuum, the residue extracted with ether, the ethereal solution neutralized with soda and dried with calcium chloride. Fractionation in vacuum gave 3.5 g fraction with b.p. 184-186° at 7 mm. From two experiments were obtained 10 g of the previously described [12] crystalline ketone (XXVI) with m.p. 81-83° [contaminated with the dehydrogenated ketone (XXII)].

2.5 g ketone (XXVI) with m.p. 81-83°, 20 ml ethyl alcohol, 10 ml water, 20 ml hydrochloric acid and 12 g amalgamated zinc were heated at 120-130° for 12 hours. The mixture was extracted with ether, the ethereal solution was washed with soda solution and dried with calcium chloride. Yield 1.2 g hydrocarbon (XXVII) with b.p. 127-128° at 4 mm; n_D^{18} 1.6035. Heating of this hydrocarbon with 1 g palladium-on-carbon (5% Pd) at 360-380° for 3 hours yielded 0.65 g hydrocarbon (XXIII) with b.p. 133-134° at 4 mm; n_D^{21} 1.6120; d_4^{20} 1.037.

13.27 mg substance: 44.84 mg CO_2; 9.47 mg H_2O. 9.57 mg substance: 32.39 mg CO_2; 6.74 mg H_2O. Found %: C 92.21, 92.36; H 8.00, 7.82. $C_{14}H_{14}$. Calculated %: C 92.30; H 7.70.

The picrate melted at 87-88° and did not give a depression with the preceding specimen.

Trans-2-vinylethinyl-2-decalol (XXX). Into a three-necked round-bottomed flask fitted with a mechanical stirrer, thermometer and dropping funnel were introduced 60 g KOH and 600 ml ether. With energetic stirring and ice cooling, addition was made over a period of 2$\frac{1}{2}$ hours of a mixture of 92 g trans-β-decalone (b.p. 92-93° at 7 mm; n_D^{18} 1.4835), 60 g vinylacetylene and 500 ml ether. The mixture was then stirred for 4 hours. The next day 100 ml water was added to the mixture, cooled with ice water. The ethereal solution was separated, washed with 1% hydrochloric acid solution and then with water, and dried with sodium sulfate. Fractionation gave 75 g trans-2-vinylethinyl-2-decalol (XXX) with b.p. 118-122° at 4 mm; n_D^{19} 1.5250 [9].

Transformation of trans-2-vinylethinyl-2-decalol (XXX) into the tricyclic ketones (XXXII and XXXVI). 20 g of the above-described vinylacetylenic alcohol (XXX) with b.p. 118-122° at 4 mm and 20 g phosphoric acid (s.g. 1.82) were heated with stirring for 12 hours at 70°. At the end of the reaction, the mixture was diluted with double the amount of water and extracted with ether; the ethereal solution was neutralized with soda and dried with calcium chloride. Yield 11 g of a mixture of ketones (XXXII) and (XXXVI) with b.p. 145-154° at 5 mm. The mixture partly crystallized. From three such experiments was obtained 10 g of the previously described [9] crystalline ketone (XXXII) with m.p. 61-63°. From the mother liquor after separation of crystalline ketone (XXXII) was obtained 8 g liquid ketone (XXXVI) with b.p. 121-122° at 3 mm; n_D^{20} 1.5390 [9].

Reduction of ketone (XXXII). 10 g ketone (XXXII) with m.p. 61-63°, 40 g ethyl alcohol, 35 g amalgamated zinc, 15 ml water and 45 ml hydrochloric acid were heated at 125-130° for 12 hours. At the end of this period, a further 40 ml hydrochloric acid was added. The product was extracted with ether, washed with soda and dried with calcium chloride. Vacuum fractionation gave 7.5 g hydrocarbon (XXXIII) with b.p. 90-91° at 3 mm; n_D^{20} 1.5080; d_4^{20} 0.9452; MR_D 59.92; calculated 59.78.

6.100 mg substance: 6.455 mg CO_2; 19.750 mg H_2O. 5.295 mg substance: 5.690 mg CO_2; 17.140 mg H_2O. Found %: C 88.30, 88.33; H 11.85, 12.00 $C_{14}H_{22}$ Calculated %: C 88.42; H 11.56.

Dehydrogenation of hydrocarbon (XXXIII). 3.5 g hydrocarbon (XXXIII) with b.p. 90-91° at 3 mm and 1.5 g palladium-on-carbon (5% Pd) were heated at 370-380° for 20 hours. Yield 1.7 g 1-methyl-5,6-benzindane (XXXIV) with b.p. 118-124° at 5 mm; n_D^{18} 1.5720. The picrate melted at 115-116° (from ethyl alcohol).

3.509 mg substance: 0.314 ml N_2 (22°, 739 mm). 3.940 mg substance: 0.343 ml N_2 (20°, 739 mm). Found %: N 10.01, 9.98. $C_{20}H_{17}O_7N_3$. Calculated %: N 10.21.

Reduction of ketone (XXXVI). After two Clemmensen reductions, in the manner described above, 8 g liquid ketone (XXXVI) (b.p. 121-122° at 3 mm) gave 1.2 g hydrocarbon (XXXVII) with b.p. 112-114° at 7 mm; n_D^{20} 1.5090; d_4^{20} 0.9465; MR_D 59.93; calculated 59.78.

8.10 mg substance: 25.99 mg CO_2; 8.43 mg H_2O. 11.35 mg substance: 36.49 mg CO_2; 11.83 mg H_2O. Found %: C 87.56, 87.73; H 11.65, 11.65. $C_{14}H_{22}$. Calculated %: C 88.42; H 11.58.

Attempted dehydrogenation of this hydrocarbon with palladium-on-carbon, either in the liquid phase or in the gas phase at 360-380°, was unsuccessful.

Dehydrogenation of the tricyclic diketone (XLI). 0.5 g diketone (XLI) with m.p. 111-112°, 0.5 g palladium-on-carbon (5% Pd) and 10 ml benzene were heated for 12 hours at 350-360°. Yield 0.2 g hydrocarbon fraction from which was obtained a picrate with m.p. 78-80° (from alcohol). A mixed sample with the picrate of 2-ethylnaphthalene, prepared by dehydrogenation of the half-ester (XI), did not give a depression.

Dehydrogenation of the tetracyclic diketone (XLII). 0.5 g diketone (XLII) with m.p. 199-201°, 0.5 g palladium-on-carbon (5% Pd) and 10 ml benzene were heated at 350-360° for 8 hours. Yield 0.1 g hydrocarbon whose picrate melted at 92-94° (from alcohol).

According to the literature [13], the picrate of 2-ethylphenanthrene (XLIII) melts at 95-96°, and the picrate of 1-ethylphenanthrene at 108-109°.

SUMMARY

Diene condensation of 1-vinyl-Δ'-cyclohexene (I) with 1,3-dimethyl-Δ'-cyclopenten-5-one (II) gives a tricyclic ketone (III), which in the reaction conditions partly isomerizes with shift of the double bond and forms the tricyclic ketone (IX). This isomerization proceeds with particular facility on heating with hydrochloric acid. The structure of ketones (III) and (IX) was proved by their transformation into known naphthalene derivatives. A study was made of the hydrogenation, dehydrogenation and reduction (Kizhner and Clemmensen methods) of ketones (III) and (IX), as well as of the corresponding saturated ketones (V) and (X). A series of new hydrocarbons containing the benzindane skeleton was synthesized.

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* See Consultants Bureau English translation, page 103 ff.

** See Consultants Bureau English translation, page 69.

*** See Consultants Bureau English translation, page 911 ff.

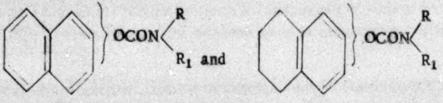
**** See Consultants Bureau English translation, page 561 ff.

***** See Consultants Bureau English translation, page 1355 ff.

N-ALKYLURETHANES AND SOME OTHER DERIVATIVES OF NAPHTHOLS AND AR-TETRALOLS

I. M. Lipovich

The purpose of the present investigation was the preparation of N-substituted urethanes of naphthols and ar-tetralols of the type of:



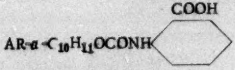
where $R = R' = CH_3$, C_2H_5, C_3H_7, C_4H_9, iso-C_5H_{11}, n-C_5H_{11}, $(CH_2CH_2Cl)_2$; or $R = H$; $R' =$ aryl or alkyl.

The starting substances were chloroformic esters of naphthols and ar-tetraols which were obtained by reaction of a benzene solution of phosgene with the respective naphthols or ar-tetralols in presence of dimethylaniline; some of them had not previously been described in the literature. The majority of the chloroformic esters proved to be stable substances and could be isolated in the pure state. α-Tetralyl chloroformate was less stable and appreciably darkened even after keeping for a short period.

Esters of N-alkylcarbamic acids (urethanes) were obtained by condensation of chloroformates with aliphatic amines. The condensation was effected by adding a benzene solution of the chloroformate to an aqueous solution of the amine (2 moles amine to 1 mole chloroformate). In these conditions the amine hydrochloride formed at the same time as the N-alkylurethane passes into aqueous solution, while the water-insolubility of the N-alkylurethane permits it to remain in solution in the benzene. Favorable conditions were thus created for the isolation of the urethanes in a sufficiently pure form. In the majority of cases the prepared urethanes were subjected to vacuum distillation, and some of them crystallized after distillation. The latter were then recrystallized. Those compounds which could not be vacuum-distilled due to decomposition were purified by recrystallization.

Apart from the above-mentioned reaction of condensation with aliphatic amines, we performed the condensation of chloroformates of α- and β-naphthols with di-(2-chloroethyl)-amine, condensation conditions being found that enabled the yield of the corresponding urethanes to reach 80% of theory (for details see the experimental part).

We were also interested in compounds obtainable by condensation of chloroformates of ar-tetralols with anthranilic acid. With this objective we prepared, apart from the known β-tetrahydronaphthyl ester of 2-carboxyphenylcarbamic acid [1], the previously undescribed α-tetrahydronaphthyl ester of 2-carboxyphenylcarbamic acid:



We also describe the α- and β-tetrahydronapthyl esters of phenylcarbamic acid since we were unable to find these compounds described in the literature. Their preparation with the help of phenylisocyanate was considerably accelerated by addition of a trace of aluminum chloride. All the derivatives of N-substituted carbamic acids that we prepared were sparingly soluble in water and very readily soluble in organic solvents. An attempt to increase the solubility in water of these compounds by preparing their salts was unsuccessful.

We also prepared the benzyl ethers of ar-tetralols by reaction of an alcoholic alkaline solution of ar-tetralols with an alcoholic solution of benzyl chloride. The benzyl ethers of ar-tetralols are high-boiling liquids which darken on standing.

EXPERIMENTAL

General Method of Preparation of N-alkylurethanes of Naphthols and ar-Tetralols

a) Preparation of chloroformates of naphthols and tetralols. To a 15% benzene solution of phosgene was gradually added, with cooling and mechanical stirring, the appropriate naphthol or tetralol dissolved in a mixture of benzene and dimethylaniline. After the solution had been added, stirring was continued for an hour at room temperature. A precipitate soon appeared: dimethylaniline hydrochloride. The substances were taken in the following proportions: 1.2 moles phosgene and 1 mole dimethylaniline per mole of naphthol or tetralol. The reaction mixture was left overnight; the next day 10% hydrochloric acid was added to the cooled solution and the aqueous layer containing the dimethylaniline hydrochloride was separated. The benzene solution, containing the chloroformate of the naphthol or tetralol, was washed with water and dried with sodium sulfate. The benzene was distilled off in vacuum and then the residue distilled in vacuum.

b) Condensation of chloroformates of naphthols and tetralols with amines. To an aqueous solution of the amine is gradually added, with cooling and mechanical stirring, a benzene solution of the chloroformate of the naphthol or the tetralol. In the majority of cases the chloroformates were used without isolating them in the pure form, i.e. they were used in the form of the benzene solution prepared as described above.

In our investigation we used mainly 50% aqueous solutions of amines (in isolated cases, 20%), for example in condensation with dimethylaniline; sometimes we used benzene solutions of amines, e.g. in condensation with n-butylamine.

After the addition of the chloroformate of the naphthol or tetralol, stirring is continued at room temperature for 2 - 2½ hours. The aqueous layer is separated from the benzene layer. The benzene solution is washed several times with water and dried with sodium sulfate before the benzene is distilled in vacuum. The residue is distilled in vacuum. A second distillation was occasionally carried out. When crystalline compounds were formed, these were recrystallized. 2 moles amine were taken per mole ester in condensation of chloroformates of naphthols and tetralols.

I. Chloroformates of Naphthols and Tetralols

1. α-Naphthyl Chloroformate: a liquid with b.p. 139-140° at 7-8 mm.

5.530 mg substance: 3.812 mg AgCl. 6.025 mg substance: 4.120 mg AgCl. 5.883 mg substance: 13.750 mg CO_2; 1.851 mg H_2O. Found %: Cl 17.05, 16.89; C 63.74; H 3.52. $C_{11}H_7O_2Cl$. Calculated %: Cl 17.19; C 63.92; H 3.39.

2. β-Naphthyl Chloroformate:* b.p. 146-147° at 8-9 mm. Rapidly crystallizes. M.p. 60-62° (from hexane).

4.368 mg substance: 3.070 mg AgCl. 6.000 mg substance: 4.170 mg AgCl. Found %: Cl 17.40, 17.19. $C_{11}H_7O_2Cl$. Calculated %: Cl 17.19.

3. α-Tetralyl Chloroformate: liquid with b.p. 143° at 12 mm. Darkens on standing.

4. β-Tetralyl Chloroformate.** Liquid with b.p. 133-134° at 7-8 mm.

3.660 mg substance: 8.451 mg CO_2; 1.670 mg H_2O. 8.574 mg substance: 5.813 mg AgCl. Found %: C 62.97; H 5.11; Cl 16.77. $C_{11}H_{11}O_2Cl$. Calculated %: C 62.70; H 5.22; Cl 16.86.

II. N-Alkyl- and N-Aryl Urethanes of Naphthols and ar-Tetralols

1. α-Naphthyl Dimethylcarbamate $\alpha\text{-}C_{10}H_7OCON(CH_3)_2$.

B.p. 191-192° at 11-12 mm. It crystallizes after lengthy standing (1 - 1½ months). Crystallization sets in rapidly after seeding. M.p. 52-55° (from ligroine). Colorless crystals, insoluble in water, soluble in organic solvents.

5.020 mg substance: 13.435 mg CO_2; 2.745 mg H_2O. 4.693 mg substance: 12.543 mg CO_2; 2.577 mg H_2O. 9.660 mg substance: 0.577 ml N_2 (20°, 730 mm). Found %: C 72.92, 72.90; H 6.12, 6.14; N 6.68. $C_{13}H_{13}O_2N$. Calculated %: C 72.55; H 6.05; N 6.50.

2. α-Naphthyl Diethylcarbamate.

From 18.5 g α-naphthol is obtained 23 g substance with b.p. 201-202° at 10-11 mm. Crystallizes quickly. Two recrystallizations from hexane give faintly colored crystals with m.p. 59-61°. Insoluble in water, very readily soluble in alcohol, ligroine and hexane.

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* This chloroformate was previously prepared in presence of quinoline [2] with m.p. 65-66°, and in presence of dimethylaniline [3] with m.p. 57°.

** β-Tetralyl chloroformate is mentioned in the patent literature but without indication of its constants and analysis.

3.619 mg substance: 9.853 mg CO_2; 2.277 mg H_2O. 3.107 mg substance: 8.417 mg CO_2; 1.885 mg H_2O. 4.578 mg substance: 1.90 ml 0.01 N H_2SO_4 for combining with the NH_3. Found %: C 74.25, 73.88; H 7.04, 6.79; N 5.81. $C_{15}H_{17}O_2N$. Calculated %: C 74.07; H 7.00; N 5.76.

3. α-Naphthyl n-Dipropylcarbamate.

A liquid with b.p. 201-202° at 7 mm was obtained. Insoluble in water, readily soluble in organic solvents. Yield 65% of theory.

5.218 mg substance: 14.413 mg CO_2; 3.610 mg H_2O. 12.911 mg substance: 4.66 ml 0.01 N H_2SO_4, for combining with NH_3. Found %: C 75.33; H 7.74; N 5.06. $C_{17}H_{21}O_2N$. Calculated %: C 75.27; H 7.75; N 5.16.

4. α-Naphthyl n-Dibutylcarbamate.

From 18.5 g α-naphthol is obtained 25 g substance with b.p. 235-237° at 10 mm. Insoluble in water, readily soluble in organic solvents.

5.196 mg substance: 14.376 mg CO_2; 3.900 mg H_2O. 7.715 mg substance: 2.62 ml 0.01 N H_2SO_4, for combining with NH_3. Found %: C 75.45; H 8.40; N 4.75. $C_{19}H_{23}O_2N$. Calculated %: C 75.79; H 8.07; N 4.91.

5. α-Naphthyl n-Butylcarbamate α-$C_{10}H_7OCONH(C_4H_9)$.

In this case the benzene solution of α-naphthyl chloroformate is first dried thoroughly and then condensed with the benzene solution of n-butylamine. After removal of the n-butylamine hydrochloride, the benzene solution is evaporated to dryness in vacuum. The residue is recrystallized from alcohol. From 9 g α-naphthyl chloroformate is obtained 4.1 g substance. Faintly colored crystals in the form of prisms with m.p. 69-72°. Insoluble in water, readily soluble in organic solvents.

4.340 mg substance: 11.749 mg CO_2; 2.853 mg H_2O. 3.882 mg substance: 10.508 mg CO_2; 2.504 mg H_2O. 5.960 mg substance: 0.317 ml N_2 (27°, 730 mm). 7.390 mg substance: 0.392 ml N_2 (27°, 730 mm). Found %: C 73.83, 73.82; H 7.35, 7.21; N 5.81, 5.79. $C_{15}H_{17}O_2N$. Calculated %: C 74.07; H 7.00; N 5.76.

6. α-Naphthyl Diisoamylcarbamate.

The compound was prepared by the general method, but after condensation of the α-naphthyl chloroformate with the aqueous solution of diisoamylamine, the sparingly-soluble diisoamylamine hydrochloride is precipitated. Consequently, prior to separation of the aqueous layer from the benzene layer, the diisoamylamine hydrochloride is removed. Further working-up is by the general method. Two vacuum distillations gave a substance with b.p. 226-227° at 6 mm. Yield 70% of theory.

6.299 mg substance: 17.748 mg CO_2; 4.832 mg H_2O. 4.199 mg substance: 1.24 ml 0.01 N H_2SO_4, for combining with NH_3. Found %: C 76.85; H 8.59; N 4.17. $C_{21}H_{29}O_2N$. Calculated %: C 77.06; H 8.87; N 4.28.

7. α-Naphthyl n-Diamylcarbamate.

Reaction conditions and procedure for separation were the same as in the preceding experiment. The pale-green product had b.p. 224-225° at 6 mm. Yield 60% of theory.

5.944 mg substance: 16.769 mg CO_2; 4.689 mg H_2O. 10.750 mg substance: 0.410 ml N_2 (20°, 733 mm). Found %: C 76.94; H 8.82; N 4.28. $C_{21}H_{29}O_2N$. Calculated %: C 77.06; H 8.87; N 4.28.

8. α-Naphthyl Di-(2-chloroethyl)-carbamate α-$C_{10}H_7OCON(CH_2CH_2Cl)_2$.

10 g di-(2-chloroethyl)amine hydrochloride is dissolved in 25 ml water and stirred with an aqueous solution of alkali (2.3 g NaOH in 15 ml water) at 0°. To the resultant solution of di-(2-chloroethyl)amine are gradually added simultaneously in the course of an hour, with good mechanical stirring and cooling to 0-5°, a chloroform solution of α-naphthyl chloroformate (1.17 g ester in 18 ml chloroform) and an alkali solution (2.5 g NaOH in 25 ml water). The chloroform solution is then separated from the aqueous layer. The chloroform is driven

off. The residue is distilled in vacuum. A product is obtained with b.p. 222-223° at 4-3 mm and very quickly crystallizing. Yield 16 g or 80% of the theoretical. After recrystallization from alcohol the m.p. is 81-83°. Colorless crystals, insoluble in water, soluble in organic solvents.

3.441 mg substance: 7.286 mg CO_2; 1.595 mg H_2O. 3.124 mg substance: 6.600 mg CO_2; 1.435 mg H_2O. 7.930 mg substance: 0.318 ml N_2 (24.0°, 728 mm). 8.620 mg substance: 0.336 ml N_2 (24.0°; 728 mm). 6.034 mg substance: 5.439 mg AgCl. Found %: C 57.74, 57.62; H 5.18, 5.14; N 4.41, 4.29; Cl 22.30. $C_{15}H_{15}O_2NCl_2$. Calculated %: C 57.69; H 4.80; N 5.49; Cl 22.75.

9. β-Naphthyl Dimethylcarbamate. *

Prepared by the general method. A 20% aqueous solution of dimethylamine was taken for the reaction. After the solvent had been driven off in vacuum, the residue crystallized. M.p. 96-98° after 3 recrystallizations from alcohol. Colorless crystals, insoluble in water, readily soluble in organic solvents.

4.011 mg substance: 10.723 mg CO_2; 2.257 mg H_2O. 7.00 mg substance: 0.397 ml N_2 (20°, 743 mm). Found %: C 72.91; H 6.29; N 6.42. $C_{13}H_{13}O_2N$. Calculated %: C 72.55; H 6.05; N 6.50.

10. β-Naphthyl Diethylcarbamate.

The compound has b.p. 203-205° at 11 mm. Rapidly crystallizes. M p. 56-58° after two recrystallizations from hexane. Colorless crystals, insoluble in water, very easily soluble in organic solvents. Yield 70% of theory.

4.420 mg substance: 11.948 mg CO_2; 2.770 mg H_2O. 3.882 mg substance: 10.501 mg CO_2; 2.395 mg H_2O. 6.890 mg substance: 2.85 ml 0.01 N H_2SO_4 for combining with NH_3. 6.834 mg substance: 2.81 ml 0.01 N H_2SO_4, for combining with NH_3. Found %: C 73.72, 73.77; H 7.01, 6.90; N 5.79, 5.75. $C_{15}H_{17}O_2N$. Calculated %: C 74.07; H 7.00; N 5.76.

11. β-Naphthyl n-Butylcarbamate $\beta\text{-}C_{10}H_7OCONH(C_4H_9)$.

Prepared in the conditions described above for α-naphthyl n-butylcarbamate. The compound is first recrystallized from a mixture of ligroine and benzene, and then from alcohol; m.p. 121-123°; forms platelets, insoluble in water, readily soluble in organic solvents.

3.772 mg substance: 10.288 mg CO_2; 2.471 mg H_2O. 3.710 mg substance: 10.059 mg CO_2; 2.379 mg H_2O. 8.320 mg substance: 0.431 ml N_2 (27.0°, 729 mm). 6.285 mg substance: 0.327 ml N_2 (25.5°, 730 mm). Found %: C 74.38, 73.95; H 7.33, 7.17; N 5.66, 5.72. $C_{15}H_{17}O_2N$. Calculated %: C 74.07; H 7.00; N 5.76.

12. β-Naphthyl Di-(2-chloroethyl)carbamate.

The reaction was performed and the compound worked up as in the case of α-naphthyl di-(2-chloroethyl)carbamate. A compound was obtained with b.p. 233-237° at 3 mm. On recrystallization from alcohol it formed small needles with m.p. 65-68°. Yield 60% of theory.

3.985 mg substance: 8.371 mg CO_2; 1.645 mg H_2O. 7.635 mg substance: 0.312 ml N_2 (24°, 728.5 mm). 7.565 mg substance: 0.310 ml N_2 (24.0°, 728.5 mm). 4.855 mg substance: 4.385 mg AgCl. Found %: C 57.28; H 4.62; N 4.50, 4.52; Cl 22.34. $C_{15}H_{15}O_2NCl_2$. Calculated %: C 57.69; H 4.80; N 4.49; Cl 22.75.

13. α-Tetrahydronaphthyl Diethylcarbamate $ar\text{-}\alpha\text{-}C_{10}H_{11}OCON(C_2H_5)_2$.

Liquid with b.p. 191-192° at 13 mm. Yield 70% of the theoretical.

3.070 mg substance: 8.218 mg CO_2; 2.309 mg H_2O. 7.385 mg substance: 0.370 ml N_2 (22°, 733 mm). Found %: C 73.01; H 8.42; N 5.59. $C_{15}H_{21}O_2N$. Calculated %: C 72.87; H 8.50; N 5.67.

14. α-Tetrahydronaphthyl n-Dibutylcarbamate.

From 18.5 g α-tetralol was obtained 20 g substance with b.p. 215-217° at 8 mm.

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* Previously obtained by reacting trimethylamine with β-naphthyl chloroformate [3], m.p. 92°.

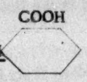
5.084 mg substance: 14.100 mg CO_2; 4.237 mg H_2O. 15.020 mg substance: 0.649 ml N_2 (21°; 726.5 mm). Found %: C 75.63; H 9.32; N 4.75. $C_{19}H_{29}O_2N$. Calculated %: C 75.25; H 9.57; N 4.62.

15. β-Tetrahydronaphthyl Diethylcarbamate.

Liquid with b.p. 192-194° at 8-9 mm. It crystallizes on standing, but sometimes the process of crystallization continues for several weeks. After two recrystallizations from alcohol it forms colorless crystals with m.p. 62-64°.

3.806 mg substance: 10.239 mg CO_2; 2.882 mg H_2O. 5.302 mg substance: 2.12 ml 0.01 N H_2SO_4, required for combining with the NH_3. Found %: C 73.36; H 8.47; N 5.60. $C_{15}H_{21}O_2N$. Calculated %: C 72.87; H 8.50; N 5.67.

16. α-Tetrahydronaphthyl 2-Carboxyphenylcarbamate ar α-$C_{10}H_{11}OCONH$



$\alpha\text{-}C_{10}H_{11}OCONH\text{-}C_6H_4\text{-}COOH$

To a benzene solution containing α-tetralyl chloroformate (prepared from 50 g α-tetralol by the above-described method) is added, with cooling and stirring, 46 g anthranilic acid. After the acid has been added, stirring is continued for several hours at room temperature and the mass is left till the next day. An aqueous solution of KOH (10 g KOH in 100 ml water) is then added, with cooling and mechanical stirring, and stirring afterwards continued for several hours. The precipitate is filtered, washed several times with hot water. After two recrystallizations from alcohol, a substance with m.p. 167-169° (with decomposition) is obtained. Insoluble in water, soluble in alcohol, acetone and chloroform.

3.583 mg substance: 9.128 mg CO_2; 1.796 mg H_2O. 3.742 mg substance: 9.530 mg CO_2; 1.820 mg H_2O. 8.668 mg substance: 0.367 ml N_2 (27.5°, 724 mm). 8.397 mg substance: 0.351 ml N_2 (26°, 724 mm). Found %: C 69.48, 69.46; H 5.60, 5.45; N 4.58, 4.58. $C_{18}H_{17}O_4N$. Calculated %: C 69.45; H 5.46; N 4.50.

17. α-Tetrahydronaphthyl Phenylcarbamate, α-$C_{10}H_{11}OCONH(C_6H_5)$.

To 20 g α-tetralol is added 20 g phenylisocyanate, solution is effected by heating, and the mass is left at room temperature for 7 days; the precipitate is then drained and washed several times with ligroine. Two recrystallizations (from alcohol-acetone and then from acetone) gave 10 g with m.p. 169-171°; fine crystals in form of needles.

3.561 mg substance: 9.998 mg CO_2; 2.015 mg H_2O. 6.674 mg substance: 0.315 ml N_2 (23°, 729 mm). 7.205 mg substance: 0.347 ml N_2 (23°, 729 mm). Found %: C 76.57; H 6.33; N 5.22, 5.33. $C_{17}H_{17}O_2N$. Calculated %: C 76.40; H 6.36; N 5.24.

18. β-Tetrahydronaphthyl Phenylcarbamate.

To 25 g β-tetralol is added 25 g phenylisocyanate, solution is effected by heating, and addition is then made of a trace of aluminum chloride. Crystallization is complete after a day. The crystals are drained and washed with ligroine. Yield 40 g unpurified substance. M.p. 151-152° after three recrystallizations from acetone; white needles.

3.065 mg substance: 8.600 mg CO_2; 1.725 mg H_2O. 8.035 mg substance: 0.388 ml N_2 (22.5°, 741 mm). 7.145 mg substance: 0.333 ml N_2 (22.5°, 743.5 mm). Found %: C 76.51; H 6.30; N 5.44, 5.27. $C_{17}H_{17}O_2N$. Calculated %: C 76.40; H 6.36; N 5.24.

19. α-Tetralyl Benzyl Ether α-$C_{10}H_{11}OCH_2C_6H_5$.

To 9.3 g KOH in 40 ml absolute alcohol is added 22.2 g α-tetralol with heating. Gradual addition is then made to the solution of an alcoholic solution of benzyl chloride (38 g benzyl chloride in 40 ml alcohol). Heating is then continued for 2½ hours. After cooling, the KCl is filtered off. The alcohol is driven off and the residue is diluted with water and extracted with ether. The ether extract is washed several times with Claisen mixture and then with water and dried with calcium chloride.

The ether is driven off and the residue distilled in vacuum. The benzyl ether of α-tetralol forms a light-yellow liquid with b.p. 195-196° at 9 mm. Color changes to cherry-red on standing. Analysis for hydroxyl group gave a negative result.

3.500 mg substance: 11.038 mg CO_2; 2.305 mg H_2O. Found %: C 86.01; H 7.36. $C_{17}H_{18}O$. Calculated %: C 85.71; H 7.56.

20. β-Tetralyl Benzyl Ether

Prepared in the above-described conditions for the benzyl ether of α-tetralol. The benzyl ether of β-tetralol is a liquid with b.p. 169-171° at 5-6 mm, insoluble in water, easily soluble in organic solvents.

4.195 mg substance: 13.215 mg CO_2; 2.784 mg H_2O. 3.624 mg substance: 11.435 mg CO_2; 2.411 mg H_2O. Found %: C 85.91, 86.05; H 7.43, 7.44. $C_{17}H_{18}O$. Calculated %: C 85.71; H 7.56.

SUMMARY

Condensation of chloroformates of naphthols and ar-tetralols with aliphatic amines yielded a series of their N-alkyurethanes not previously described in the literature. Several other derivatives of naphthols and ar-tetralols, likewise undescribed in the literature, were also prepared.

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THE PROBLEM OF THE SYNTHESIS OF SUBSTITUTED CYSTEINES

II. THE POSSIBILITY OF FUSING SUBSTITUTED HYDANTOINS FOR THE PREPARATION OF β,β-DIPHENYLCYSTEINE

T. A. Favorskaya and L. A. Remizova

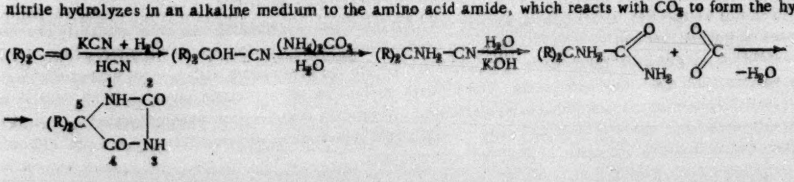
In the first communication [1], it was shown that the reaction of diphenylacetaldehyde and diphenylglycolaldehyde with KCN and NH_4Cl in aqueous ethereal solution proceeds mainly with formation of hydroxy- and dihydroxynitriles, the yield of the corresponding amino- and hydroxyaminonitriles being very small. Moreover, hydrolysis of the isolated hydrochloride of α-amino-β,β-diphenylpropionitrile showed that this compound is very unstable and readily undergoes — both in an acid and an alkaline medium — various transformations, leading to shortening of the chain of carbon atoms, to formation of simpler compounds (benzhydrol, diphenylacetaldehyde and diphenylacetic acid). An attempt was therefore made to prepare α-amino-β,β-diphenylpropionic acid by another route.

One of the methods of synthesis of α-amino acids is the hydrolysis of the corresponding substituted hydantoins.

In 1934 Bucherer and co-workers [2,3] developed a method of preparation of hydantoins, starting from aldehydes and ketones which were reacted with KCN and ammonium carbonate in aqueous alcoholic medium. By replacing the aldehydes by their bisulfite derivatives, the authors avoided the resinification which usually occurs when the reaction is carried out with the aldehydes themselves. The authors believe that hydantoins are formed via the following series of intermediates: hydroxynitrile, aminonitrile, and carbamic acid; the latter is unstable and undergoes intramolecular rearrangement, in the instant of its formation, into another unstable compound which in turn rearranges into the stable hydantoin.

Other authors [4] had investigated the preparation of various hydantoins by a similar method about the same time as Bucherer, but using a higher temperature and a pressure of 2-8 atmospheres. They believe that the carbonyl compound reacts with KCN and ammonium carbonate in its enol form. Their reason for so thinking is that ketones whose carbonyl group is linked to two aromatic radicals, e.g. benzophenone, are recovered unchanged in this reaction, whereas benzylphenyl ketone — which is capable of enolization — forms an hydantoin with good yield. Recently, however, conditions were established [5] for the preparation from diaryl ketones of the corresponding 5,5-diarylhydantoins in over 90% yield; this shows that enolization is not an essential condition for reaction of carbonyl compounds with potassium cyanide.

The formation of a hydantoin may be explained more simply by assuming that the initially formed aminonitrile hydrolyzes in an alkaline medium to the amino acid amide, which reacts with CO_2 to form the hydantoin.

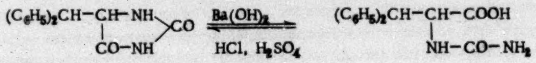


In recent years investigators have shown greatly increased interest in the synthesis of hydantoins because some of these, for example, 5,5-ethylphenylhydantoin (nirvanol) and 5,5-diphenylhydantoin (dilactin) possess an anticonvulsant activity and are used for treatment of epilepsy [6]. Moreover, substituted hydantoins serve as a source of α-amino acids, formed as a result of their hydrolysis. However, the hydrolysis of hydantoins is not so simple because hydantoins are stable toward dilute acids; even boiling concentrated hydrochloric acid has no action on them, and 40% sulfuric acid only partly hydrolyzes them. Complete hydrolysis can only be effected with 60% sulfuric acid by heating to 120-130° [2]. In this way Bucherer succeeded in preparing the corresponding amino acids from 5,5-dimethyl- and 5-methyl-5-ethylhydantoins.

Heating of hydantoins with dilute caustic alkalies [7] brings about hydration of the ring and formation of hydantoic acids. From the latter the hydantoins can be regenerated by heating with dilute mineral acids [8]. Sometimes a hydantoic acid can be converted into an amino acid; thus, N. A. Menshutkin [9] obtained glycine by heating hydantoic acid in a sealed tube with hydriodic acid for 20 hours at 160-170°. The best method of hydrolysis of hydantoins — and the one in use at the present time — is heating of hydantoins with barium hydroxide in aqueous solution in a sealed tube. By this method hydantoins have been converted into such amino acids as lysine $NH_2-(CH_2)_4-CHNH_2-COOH$ [10,11]; serine $HOCH_2-CH(NH_2)-COOH$, cysteine $HS-CH_2-CH(NH_2)-$ $-COOH$ [12], methionine [13] $CH_3SCH_2-CH_2-CH(NH_2)COOH$, etc.

After failing to prepare α-amino-β,β-diphenylpropionic acid by the action of KCN and NH_4Cl on diphenylacetaldehyde, we decided to attempt to prepare this acid by hydrolysis of 5-benzhydrylhydantoin (I). This hydantoin was prepared in 1950 [6] in 44% yield by the reaction of diphenylacetaldehyde with KCN and ammonium carbonate when heated at 110° under pressure. The author prepared diphenylacetaldehyde by a rather complex method starting from formaldehyde.

We prepared the hydantoin in 75% yield by Bucherer's method [2,3]. Heating of the hydantoin with 60% sulfuric acid at 130-140° for an hour had no result apart from formation of resins. The hydantoin was recovered unchanged after prolonged boiling with concentrated hydrochloric acid, as well as after boiling with hydriodic acid in presence of acetic anhydride [12]. Boiling of the hydantoin with an aqueous solution of barium hydroxide at atmospheric pressure resulted in a quantitative yield of the previously unknown α-benzhydrylhydantoic acid (II). Heating of the hydantoin with barium hydroxide in a sealed tube at 140° for 15 minutes gave the same hydantoic acid but in lower yield; α-benzhydrylhydantoic acid is quantitatively reconverted into the hydantoin when heated with dilute and concentrated hydrochloric acid or with dilute sulfuric acid.



(I) (II)

Although we thus failed to obtain α-amino-β,β-diphenylpropionic acid from 5-benzhydrylhydantoin, we decided to attempt to introduce the sulfhydryl group into the 5-benzhydrylhydantoin molecule and thereby to obtain the mercaptohydantoin and therefrom the mercaptohydantoic acid. It should be interesting to prepare such compounds from the standpoint of their pharmacological properties. With this aim, it was decided to prepare mercaptodiphenylacetaldehyde and to convert this into the hydantoin.

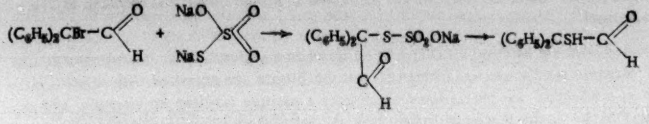
Introduction of the mercapto group into the molecule of an aliphatic compound is usually effected by reacting hydrosulfides of alkali metals with halogen derivatives of these compounds [14, 15, 16, 17]. V. M. Rodionov [18], however, recommends treating benzyl chloride with sodium thiosulfate in aqueous alcoholic solution to form benzylmercaptan. The reaction proceeds with formation of the intermediate known as Bunte's salt, treatment of which with dilute sulfuric acid decomposes it to benzylmercaptan.

We resolved to apply this method to the preparation of mercaptodiphenylacetaldehyde. The substance obtained by this reaction was distilled in high vacuum. Its color was emerald-green; it had a repulsive, clinging odor; the reaction to litmus was neutral, and it gave a positive reaction for sulfur. On standing, the color gradually changed from deep-green to light-yellow and the reaction to litmus changed from neutral to acid. Moreover, the substance gave a positive reaction for the aldehyde group, but a qualitative test for the mercapto group with nascent nitrous acid was negative; the substance did not titrate with iodine. Quantitative analysis for sulfur (Carius) gave only a 2% content in place of the 14% calculated for mercaptodiphenylacetaldehyde. Treatment with 2,4-dinitrophenylhydrazine gave two 2,4-dinitrophenylhydrazones: one with m.p. 237° (the 2,4-dinitrophenylhydrazone of benzophenone) and one with m. p. 145-146° (the 2,4-dinitrophenylhydrazone of diphenylacetaldehyde).

On the basis of these data we may say that although the substance distills within a range of one degree, it is a mixture of which one of the components is benzophenone. It was impossible to judge whether the other substance was diphenylacetaldehyde or thiodiphenylacetaldehyde, or a mixture of these, on the basis solely of preparation of the 2,4-dinitrophenylhydrazone of diphenylacetaldehyde because both aldehydes give one and the same 2,4-dinitrophenylhydrazone. The presence of the thioaldehyde was inferred from the emerald color and the very repulsive odor. Moreover, the development of an acid reaction and the color change on standing pointed to the easy oxidizability of the substance, which is characteristic of thioaldehydes.

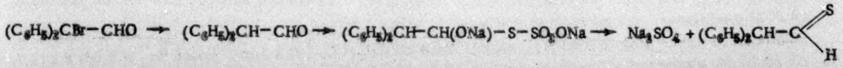
We know [19] that aldehydes can react with sodium thiosulfate not only with formation of mercapto derivatives; in an anhydrous medium they react to form thioaldehydes. In our case, evidently, the reaction of bromodiphenylacetaldehyde with sodium thiosulfate proceeded in several directions.

On the one hand the reaction probably proceeded, according to Rodionov's mechanism, with formation of the mercaptoaldehyde:



The mercaptoaldehyde decomposed into thiobenzophenone and formaldehyde, while the thiobenzophenone (readily oxidizable in the air) gave benzophenone which was detected in the reaction products.

At the same time the sodium thiosulfate acted on the bromodiphenylacetaldehyde as a reducing agent and transformed it into diphenylacetaldehyde, whose aldehyde group entered into reaction with $Na_2S_2O_3$ to form the thioaldehyde:



This second direction of the reaction accounts for the presence of diphenylacetaldehyde and thiodiphenylacetaldehyde in the reaction products.

After failing to obtain the mercaptoaldehyde by Rodionov's method, we decided to attempt its preparation by the action of NaSH on bromodiphenylacetaldehyde in an anhydrous medium. With this objective, freshly prepared sodium hydrosulfide, suspended in dry benzene, was slowly stirred into a benzene solution of bromodiphenylacetaldehyde. The reaction was performed at room temperature. Addition of the hydrosulfide was accompanied by release of heat and development of a dark-blue color. The reaction product was distilled in high vacuum to give a liquid with a blue color and a neutral reaction to litmus. The blue color disappeared fairly quickly on standing; the product did not have a repulsive odor and did not give a reaction for sulfur. Treatment with 2,4-dinitrophenylhydrazine gave two 2,4-dinitrophenylhydrazones corresponding to derivatives of benzophenone and diphenylacetaldehyde. These results showed that in this case also the bromodiphenylacetaldehyde had been partly reduced to diphenylacetaldehyde. The formation of benzophenone in both cases shows that (in both cases) there is, so to speak, partial replacement of bromine in bromodiphenylacetaldehyde by the mercapto group, but in the reaction conditions the mercaptodiphenylacetaldehyde is unstable and behaves like the derivatives of diphenylglycolaldehyde and diphenylacetaldehyde that we have previously studied [9] in decomposing with formation of thiobenzophenone, which oxidizes to benzophenone in the air. The deep-blue color, characteristic of thioketones, is indicative of the presence of thiobenzophenone in the reaction products.

EXPERIMENTAL

Preparation of 5-Benzhydrylhydantoin

In a round-bottomed flask are placed 22 g KCN (2 moles), 64 g ammonium carbonate (4 moles) and 200 ml 50% ethyl alcohol. Gradual addition is then made, with stirring, of 40 g of the bisulfite derivative of diphenylacetaldehyde. The reaction mixture is heated on the water bath so that the temperature in the flask is 50-55°; after 6 hours' heating at this temperature, the temperature is raised to 70-75° to decompose the excess of ammonium carbonate. After cooling of the solution, the formed hydantoin crystallizes. The filtered hydantoin is washed with water to remove inorganic impurities. Weight of the hydantoin 16 g. The filtrate deposited a further 11.3 g on standing. M.p. 218-219° from aqueous alcohol. Yield 26.2 g or 74%.

According to the literature the m.p. is 221°.

0.0738 g substance: 6.8 ml N_2 (15°, 754.9 mm). 0.1595 g substance; 11.98 g dioxane: Δt 0.315°.
Found %: N 10.65; M 234.6. $C_{16}H_{14}O_2N_2$. Calculated %: N 10.52; M 266.

Due to the insolubility of the prepared hydantoin in benzene, the molecular weight was determined in dioxane; the dioxane constant for phenylacetic acid was previously determined.

Hydrolysis of 5-Benzhydrylhydantoin

2.5 g 5-benzhydrylhydantoin was heated with 100 ml 60% sulfuric acid for an hour at 120-130°. After cooling, the sulfuric acid was neutralized with the calculated amount of $BaCO_3$; the precipitate was filtered and washed with ether. Removal of the ether left a small amount of resin. The aqueous solution had the mousy odor characteristic of acetamide, but no organic products whatever could be isolated from it. In the specified conditions, therefore, the 5-benzhydrylhydantoin had decomposed. When the reaction was performed in milder conditions (heating at 100°) the hydantoin was recovered undhanged.

2 g hydantoin was heated with 8 g $Ba(OH)_2 \cdot 8H_2O$ and 50 ml water in a sealed tube for 15 minutes at 136°. After opening the tube, the inorganic precipitate was filtered off and the filtrate was acidified with dilute hydrochloric acid until weakly acid; a substance was precipitated which gave a positive reaction for nitrogen, had an acid reaction, and melted at 178-180° before recrystallization; from the residual solution was isolated a small amount of neutral product of decomposition not containing nitrogen and melting at 74-76°; it was not further investigated. In the next experiment, in order to avoid decomposition of the 5-benzhydrylhydantoin, 8 g of the latter was heated with 30 g $Ba(OH)_2 \cdot 8\,H_2O$ and 150 ml water under a reflux condenser at 100° for an hour. Acidification with dilute hydrochloric acid brought down 8.45 g of a substance melting at 197-198° after recrystallization from aqueous alcohol. A mixed melting point determination with the acid prepared in the previous experiment did not give a depression: m.p. 185-186°.

0.0710 g substance: 6.1 ml N_2 (19°, 766 mm). 0.0919 g substance: 3.5 ml NaOH ($\underline{F}$ 0.9387). 0.0745 g substance: 0.0206 g Ag; 0.0821 g substance: 25.8 ml CH_4 (17°, 762.5 mm). Found %: N 9.90; $\underline{E}$ 279.7; % Ag 27.65; number of active hydrogen atoms 3.7. $C_{16}H_{16}O_3N_2$. Calculated %: N 9.85; $\underline{E}$ 284, number of active hydrogen atoms 4. $C_{16}H_{15}O_3N_2Ag$. Calculated %: Ag 27.62.

The analytical results show that alkaline hydrolysis of 5-benzhydrylhydantoin gave α-benzhydrylhydantoic acid. The anticipated α-amino acid was not formed either on acid or alkaline hydrolysis.

The transformations of α-benzhydrylhydantoic acid in acid and alkaline media were studied.

When boiled with 20% hydrochloric acid and with 20% sulfuric acid, 2 g of the acid gave 1.7 g 5-benzhydrylhydantoin. Boiling of 1 g of the acid with concentrated hydrochloric acid gave 0.8 g of the hydantoin. When the acid was boiled with aqueous $Ba(OH)_2$ for 5 hours, it was quantitatively recovered unchanged.

Preparation of Mercaptophenylacetaldehyde by Rodionov's Method [18]

A reaction mixture comprising 40 g bromodiphenylacetaldehyde dissolved in 80 ml, 96% alcohol and a solution of 41 g sodium thiosulfate in 40 ml water was heated with stirring at the boil for 22 hours until the Beilstein reaction for chlorine was negative. During the reaction an oil settled out and sulfur was liberated. At the conclusion of the heating a stream of carbon dioxide was passed through the reaction flask, after which 90 ml 45% sulfuric acid was added; this caused a considerable volume of oily liquid to separate. The substance was extracted with ether and dried with sodium sulfate. After driving off the ether, the substance was distilled in high vacuum. In the first fractionation the substance boiled at 125-134°.

A second fractionation gave the following fractions: 1) to 120°, a few drops; 2) 122°, 10 g; 3) 123-132° 1.5 g; decomposition of the substance and separation of sulfur were observed.

The second fraction with an emerald-green color had a most unpleasant and very persistent odor; it gave positive reactions for sulfur and aldehyde group and was neutral to litmus. On standing in a closed vessel, the color gradually changed from green to light-yellow. At the same time the reaction to litmus became acid. The substance did not give a color reaction with nascent nitrous acid and did not titrate with iodine, which indicated the absence of the SH group.

0.1046 g substance: 0.0156 g $BaSO_4$. 0.0969 g substance: 1.7 ml CH_4 (17°, 764.7 mm). 0.0926 g substance; 14.85 g benzene: Δt 0.155°. Found %: S 2.04; number of active hydrogen atoms 0.2090; M 206.3. $C_{14}H_{12}OS$. Calculated %: S 14.03, number of active hydrogen atoms 1; M 228.

The data showed that the substance that distilled over within a range of one degree is a mixture and not a pure compound.

Preparation of 2,4-dinitrophenylhydrazone of substance with b.p. 122° at a pressure of less than 1 mm. To a freshly prepared solution of 2,4-dinitrophenylhydrazine was added 0.5 g substance dissolved in alcohol. Almost at once a dark-red precipitate was formed; after a short time another 2,4-dinitrophenylhydrazone began to separate in the form of yellow needles. On recrystallization from 96% alcohol, the dark-red 2,4-dinitrophenylhydrazone did not dissolve whereas the light-yellow hydrazone dissolved fairly quickly. The light-yellow substance melted at 145-146° and did not give a depression with an authentic sample of diphenylacetaldehyde 2,4-dinitrophenylhydrazone.

The dark-red 2,4-dinitrophenylhydrazone was recrystallized from ethylacetoacetate, m.p. 235-236°; a mixed test with benzophenone 2,4-dinitrophenylhydrazone did not give a depression. In view of the fact that the substance changed from neutral to acid on standing, it was oxidized with $KMnO_4$ solution. Oxidation of 3.6 g substance with b.p. 122° at a pressure of less than 1 mm consumed 2.28 g permanganate. The neutral product obtained was benzophenone (1.3 g); in the acid products of oxidation were found diphenylacetic acid (m.p. 144-145°) and a small admixture of benzoic acid; these were separated by fractional distillation. It follows that the substance with b.p. 122° in high vacuum consisted of benzophenone and a mixture of diphenylacetaldehyde and thiodiphenylacetaldehyde.

Preparation of the Mercaptoaldehyde by Reaction of Bromodiphenylacetaldehyde with NaSH

To 20 g bromodiphenylacetaldehyde dissolved in 50 ml dry benzene was added, in small portions, freshly prepared NaSH [20] suspended in benzene. During the addition heat was developed and the color became dark-blue. The end of the reaction was indicated by absence of heat development when fresh portions of NaSH were added and by a negative reaction for halogen. The benzene solution was decanted from the inorganic precipitate; the precipitate was washed with benzene and the wash liquor added to the main solution. After driving off the benzene, the substance was distilled in high vacuum to give 8 g blue liquid with b.p. 127-138° at a pressure below 1 mm. A second distillation at a pressure of less than 1 mm gave 2 fractions: 1) 123-133°, 3.45 g; 2) 134-138°, 1.25 g. Both fractions were blue, readily mobile liquids not giving a positive reaction for sulfur and with a neutral reaction to litmus. With 2,4-dinitrophenylhydrazine both fractions gave two 2,4-dinitrophenylhydrazones: benzophenone hydrazone (main product) and a small quantity of the hydrazone of diphenylacetaldehyde. Mixed tests with the authentic 2,4-dinitrophenylhydrazones gave no depression. The mass remaining after distillation gave a qualitative reaction for sulfur and the aldehyde group, but did not give a color reaction with nascent nitrous acid. Treatment with 2,4-dinitrophenylhydrazine gave a small amount of the 2,4-dinitrophenylhydrazone of diphenylacetaldehyde.

Consequently, the reaction with NaSH also failed to give mercaptophenylacetaldehyde, although the reaction was performed in very mild conditions: the reaction temperature did not rise above 30°. In the instant of its formation the mercaptophenylacetaldehyde is apparently decomposed into thiobenzophenone and formaldehyde, and the thiobenzophenone is oxidized to benzophenone by oxygen from the air. Furthermore, NaSH acted on bromodiphenylacetaldehyde as a reducing agent and reduced it to diphenylacetaldehyde, which was also detected in the reaction products.

SUMMARY

1. Preparations were carried out of 5-benzhydrylhydantoin (in 75% yield by Bucherer's method) and of α-benzhydrylhydantoic acid which had not previously been known. Their transformations in acid and alkaline media were studied.

2. Substitution of the halogen in bromodiphenylacetaldehyde by the mercapto group by the action of NaSH in an anhydrous medium was studied.

3. It was shown that the resultant mercaptodiphenylacetaldehyde is unstable and decomposes with formation of thiobenzophenone which undergoes oxidation to benzophenone. Moreover, NaSH acts on bromodiphenylacetaldehyde as a reducing agent and reduces it to diphenylacetaldehyde.

The reaction of bromodiphenylacetaldehyde with sodium thiosulfate by Rodionov's method proceeded in two directions: with formation of mercaptodiphenylacetaldehyde (which decomposed to thiobenzophenone, which oxidized to benzophenone) and with formation of diphenylacetaldehyde and thiodiphenylacetaldehyde. The latter is also readily oxidized in the air.

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SYNTHESIS OF 2,3-DISUBSTITUTED QUINUCLIDINES

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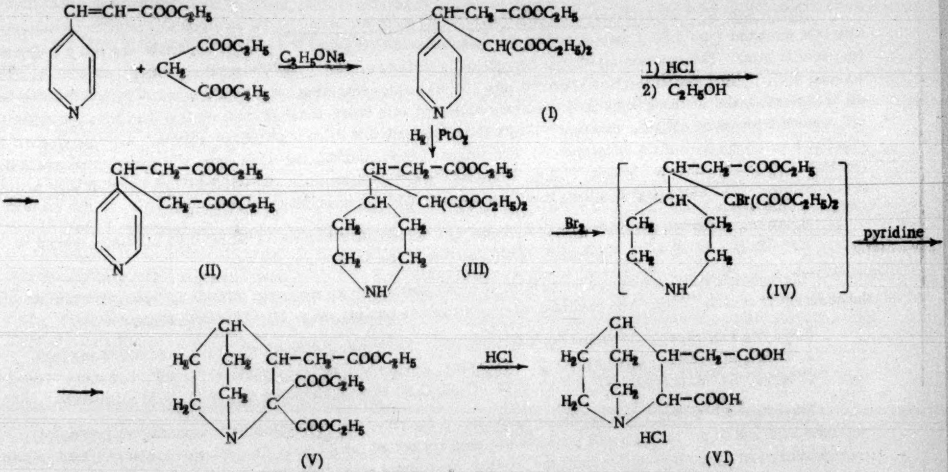
Substituted quinuclidines are of undoubted interest as a possible source of therapeutic substances. Up to recently, however, compounds of this series have not been subjected to extensive biological investigation due to the complexity of their preparation [1].

One of us, in collaboration with Dorokhova, recently developed a simple synthesis of 2-quinuclidinecarboxylic acid and its derivatives [2] and thus made possible a more extensive study of the biological and chemical properties of compounds of this class.

Continuing our work in this direction, we have realized the synthesis of [2-carboxyquinuclidyl-(3)]-acetic acid, some of its derivatives and products of their transformation, which are described in this paper.

2,3-Disubstituted quinuclidines have not been described in the literature; apart, therefore, from the possibility of investigating their biological properties, a study of the chemical properties of compounds of this series was also a matter of interest.

Our synthesis of [2-carboxyquinuclidyl-(3)]-acetic acid may be represented by the following scheme:


CH=CH−COOC₂H₅
+ CH₂
COOC₂H₅
COOC₂H₅
N
C₂H₅ONa
CH−CH₂−COOC₂H₅
CH(COOC₂H₅)₂
N
(I)
1) HCl
2) C₂H₅OH
H₂ | PtO₂
CH−CH₂−COOC₂H₅
CH₂−COOC₂H₅
N
(II)
CH−CH₂−COOC₂H₅
CH
CH(COOC₂H₅)₂
CH₂
CH₂
CH₂
CH₂
NH
(III)
Br₂
CH−CH₂−COOC₂H₅
CH
CBr(COOC₂H₅)₂
CH₂
CH₂
CH₂
CH₂
NH
(IV)
pyridine
CH
H₂C
CH₂
CH−CH₂−COOC₂H₅
COOC₂H₅
CH₂
H₂C
C
COOC₂H₅
N
(V)
HCl
CH
H₂C
CH₂
CH−CH₂−COOH
CH₂
H₂C
CH−COOH
N
HCl
(VI)

Preparation of the ethyl ester of β-dicarbethoxymethyl-β-[pyridyl-(4)]-propionic acid (I), the starting material of the present synthesis, was effected with the help of Michael's reaction. Ethyl malonate readily reacts with the equivalent amount of ethyl β-[pyridyl-(4)]-acrylate in presence of sodium ethylate in alcoholic solution. The reaction is completed at room temperature in 5-6 hours or at 60° in one hour. (I) is formed in a yield of 94% of the theoretical. Substance (I) is a viscous liquid, partly decomposing on distillation in vacuum. The latter operation is unnecessary because reaction product (I) is obtained in complete analytical purity in the conditions detailed in the experimental part.

Boiling of (I) with concentrated hydrochloric acid gives β-[pyridyl-(4)]-glutaric acid, which was identified in the form of its diethyl ester (II).

The hydrochloride of (I) is readily reduced to the corresponding piperidine derivative (III) in presence of Adams platinum catalyst at room temperature in alcoholic solution.

In the same conditions as for preparation of 2-quinuclidinecarboxylic acid [2], β-dicarbethoxymethyl-β-[piperidyl-(4)]-propionic ester is then converted into the ethyl ester of β-dicarbethoxybromomethyl-β-[piperidyl-(4)]-propionic acid (IV) and then into the ethyl ester of [2,2-dicarbethoxyquinuclidyl-(3)]-acetic acid (V). The latter is transformed by prolonged digestion with concentrated hydrochloric acid into [2-carboxyquinuclidyl-(3)]-acetic acid hydrochloride (VI). The free acid is easily separated by treating the alcoholic solution of (VI) with the calculated amount of alcoholic solution of ammonia. The free acid is substantially insoluble in absolute alcohol, and it therefore separates by this treatment from sufficiently dilute solutions in the analytically pure form. Separation of the free acid from its hydrochloride via the silver salt was difficult to effect in practice because of the poor solubility of the silver salt in water.

The diethyl ester of [2-carboxyquinuclidyl-(3)]-acetic acid may be prepared by reaction of the dichloroanhydride of the acid with alcohol or by two heatings of the hydrochloride of the acid with a 5% alcoholic solution of hydrogen chloride. In both cases the yield of diester is about 85%, but the second method gives a purer product.

The diethyl ester of [2-carboxyquinuclidyl-(3)]-acetic acid is reduced with the help of lithium aluminum hydride with formation of 2-hydroxymethyl-3-(β-hydroxyethyl)-quinuclidine. The obtained glycol readily reacts with thionyl chloride to form 2-chloromethyl-3-(β-chloroethyl)-quinuclidine, a colorless, mobile liquid. This compound is transformed on standing into a spongy white mass, insoluble in ether. Polymeric products of the nature of quaternary salts are apparently formed. This process proceeds much more quickly with heating; thus, when pure 2-chloromethyl-3-(β-chloroethyl)-quinuclidine is distilled in vacuum, about 50% of it is converted into the polymer.

Heating of the hydrochloride of the dichloroanhydride of [2-carboxyquinuclidyl-(3)]-acetic acid with diethylaminoethanol gives the corresponding diester.

EXPERIMENTAL

Ethyl Ester of β-Dicarbethoxymethyl-β-[pyridyl-(4)]-propionic Acid (I). To an alcoholic solution of sodium ethylate prepared from 1.25 g sodium and 20 ml absolute alcohol is added 8.7 g ethyl malonate and 9.6 g β-[pyridyl-(4)]-acrylic ester. The reaction mixture is energetically stirred until a homogeneous mass is formed, and then heated for an hour at 60°. The cooled solution is poured into 100 ml water containing 3.5 g acetic acid. The precipitated heavy oil is separated, the aqueous layer is exhaustively extracted with ether, the ether extract is mixed with the separated oil, washed with water until the ethereal solution is decolorized, and dried with sodium sulfate. After driving off the ether and removing its last traces in vacuum, the residue is a viscous oil, the ethyl ester of β-dicarbethoxymethyl-β-[pyridyl-(4)]-propionic acid. Weight 17.2 g. Yield 94.2% of the theoretical. B.P. 173-175° at 0.2 mm with partial decomposition. The compound dissolves readily in organic solvents, insoluble in water.

3.442 mg substance: 7.635 mg CO_2; 2.059 mg H_2O. 5.088 mg substance: 1.64 ml 0.01 N H_2SO_4. Found %: C60.53; H 6.69; N 4.51. $C_{17}H_{23}O_6N$. Calculated %: C 60.55; H 6.82; N 4.15.

The hydrochloride is prepared by treating the compound with an alcoholic solution of hydrogen chloride until the reaction is acid to Congo. The resultant oil crystallizes on cooling. M.p. 121-122° (from alcohol-ether).

3.261 mg substance: 6.563 mg CO_2; 1.951 mg H_2O. 3.852 mg substance. 7.759 mg CO_2; 2.232 mg H_2O. 9.720 mg substance: 0.309 ml N_2 (22°, 749 mm). 9.450 mg substance: 0.302 ml N_2 (22°, 749 mm); Found %: C 54.92, 54.96; H 6.69, 6.51, N 3.62, 3.64. $C_{17}H_{23}O_6N \cdot HCl$. Calculated %: C 54.63; H 6.43; N 3.75.

Ethyl Ester of β-[Pyridyl(4)]-glutaric Acid (II). 4.4 g ethyl ester of β-dicarbethoxymethyl-β-[pyridyl(4)]-propionic acid and 44 ml concentrated hydrochloric acid are boiled for 8 hours. The solution is then filtered to free it from turbidity and evaporated in vacuum; the residual oil is dried by adding alcohol and distilling it off (this process is repeated two more times). To the resultant hydrochloride of β-[pyridyl-(4)]-glutaric acid is added 35 ml 5% alcoholic solution of hydrogen chloride, and the reaction mass is heated at the boil for 3 hours. The alcohol is driven off in vacuum; the residue is treated with 50% potassium carbonate solution and extracted with ether. The ethereal solution is dried with potassium carbonate. After driving off the ether the substance is distilled in vaccum. B.p. 146-148° at 0.2 mm. Yield 2.92 g or 84.4% of the theoretical. Colorless, viscous liquid, soluble in organic solvents, insoluble in water.

4.430 mg substance: 10.270 mg CO_2; 2.902 mg H_2O. 4.978 mg substance: 1.87 ml 0.01 N H_2SO_4. Found %: C 63.27; H 7.33; N 5.25. $C_{14}H_{19}O_4N$. Calculated %: C 63.40; H 7.17; N 5.28.

Ethyl Ester of β-Dicarbethoxymethyl-β-[piperidyl-(4)] propionic Acid (III). A solution of 47.8 g ethyl β-dicarbethoxy methyl-β-[pyridyl-(4)]-propionate hydrochloride in 330 ml absolute alcohol is reduced at room temperature in presence of 1 g platinum oxide. After absorption of the theoretical amount of hydrogen (40-45 hours), the catalyst is filtered off and the filtrate evaporated in vacuum. The residual caramel-like mass is the hydrochloride of ethyl β-dicarbethoxymethyl-β-[piperidyl-(4)]-propionate. Yield quantitative.

The base which separates on treatment of the hydrochloride with 50% potassium carbonate solution changes into an undistillable foamy mass when heated in vacuum, apparently a lactam. The reduction product was characterized by preparation of the ethyl ester of β-dicarbethoxymethyl-β-[N-acetylpiperidyl-(4)]-propionic acid. Acetylation is effected in the following manner. Ethyl β-dicarbethoxymethyl-β-[piperidyl-(4)]-propionate and 5 times the amount of acetic anhydride are heated 1 hour on a boiling water bath. The acetic anhydride is distilled off, the residue dissolved in ether, the ether solution washed with aqueous sodium bicarbonate and dried with potassium carbonate. After removal of the ether, the residue is distilled in vacuum. B.p. 206-207° at 0.3 mm. Viscous liquid with a greenish tint, readily soluble in organic solvents, insoluble in water.

7.634 mg substance: 16.595 mg CO_2; 5.501 mg H_2O. 17.000 mg substance: 0.573 ml N_2 (25°, 726 mm). Found %: C 59.32; H 8.06; N 3.69. $C_{19}H_{31}O_7N$. Calculated %: C 59.22; H 8.05; N 3.64.

Ethyl [2,2-Dicarbethoxyquinuclidyl-(3)]-acetate (V). The hydrochloride of β-dicarbethoxymethyl-β-[piperidyl-(4)]-propionic ester prepared by reduction of 47.8 g of the corresponding pyridine derivative is dissolved in 150 ml dry chloroform. To the solution is added a solution of 20.4 g bromine in 154 ml chloroform at room temperature with good stirring over a period of 8 hours. The reaction mass is allowed to stand for another 12-14 hours; during this period the solution is completely decolorized; the chloroform is then removed in vacuum. The residue is dissolved in 140 ml water, the same volume of 50% potassium carbonate solution is added, and the separated oil is extracted with ether. Without drying, the ethereal solution of β-dicarbethoxybromomethyl-β-[piperidyl-(4)]-propionic ester is evaporated in vacuum. The residual oil is digested for 2 hours with 390 ml pyridine; the reaction mass acquires a dark-brown color. The pyridine is distilled off; the residual dark-brown, viscous oil is well stirred with 50% potassium carbonate solution and extracted with ether. The ethereal solution is dried with potassium carbonate, the ether is driven off, and the residue distilled in vacuum. Yield 31.45 g ethyl ester of [2,2-dicarbethoxyquinuclidyl-(3)-acetic acid with b.p. 147-148° at 0.25 mm. A colorless, mobile liquid, readily soluble in water and organic solvents. The yield is 72% of the theoretical.

d_4^{20} 1.134; n_D^{20} 1.4793; MR_D 85.30. $C_{17}H_{27}O_6N$. Calculated: MR_D 85.20.

Methoiodide of ethyl [2,2-dicarbethoxyquinuclidyl-(3)]-acetate; white, lustrous platelets, readily soluble in water and alcohol; insoluble in ether. M.p. 139-141° (from alcohol-ether).

5.424 mg substance: 6.75 ml 0.02 N $Na_2S_2O_3$. 6.399 mg substance: 1.28 ml 0.01 N H_2SO_4. 8.378 mg substance: 1.57 ml 0.01 N H_2SO_4. Found %: I 26.33; N 2.80, 2.62. $C_{18}H_{30}O_6NI$. Calculated %: I 26.29; N 2.90.

Hydrochloride of [2-Carboxyquinuclidyl-(3)]-acetic Acid (VI). 27.5 g ethyl [2,2-dicarbethoxyquinuclidyl-(3)-acetate and 270 ml concentrated hydrochloric acid are heated at the boil for 16 hours. The hydrochloric acid solution is then decolorized with carbon and evaporated on the water bath until crystallization begins. The lustrous, white needles of the hydrochloride of [2-carboxyquinuclidyl-(3)]-acetic acid come down on cooling and are carefully drained at the pump and washed with acetone. The filtrate is concentrated in vacuum to a slurry, diluted with acetone, filtered, and washed with acetone. A further amount of hydrochloride is thus separated and is added to the main crop. Total yield 18.4 g or 91.5% of the theoretical. White crystals, readily soluble in water, poorly soluble in hot alcohol, insoluble in cold alcohol, acetone, and ether. M.p. 253-254° (with decomposition).

For analysis, part of the substance is dissolved in hot absolute alcohol and reprecipitated from solution with cold ether. M.p. 254-255° (with decomposition).

3.060 mg substance: 5.417 mg CO_2; 1.822 mg H_2O. 3.068 mg substance: 5.405 mg CO_2; 1.839 mg H_2O. 4.401 mg substance: 2.574 mg AgCl. 5.339 mg substance: 3.138 mg AgCl. Found %: C 48.31, 48.08; H 6.66, 6.70; Cl 14.48, 14.54. $C_{10}H_{15}O_4N \cdot HCl$. Calculated %: C 48.10; H 6.42; Cl 14.62.

[2-Carboxyquinuclidyl-(3)]-acetic Acid. a) 0.4 g [2-carboxyquinuclidyl-(3)]-acetic acid hydrochloride, 1.1 g silver oxide and 6 ml water are shaken for 2 hours. The mass is diluted with 40 ml water, brought to the boil, filtered and washed with 45 ml hot water. The filtrate is saturated with hydrogen sulfide, the precipitated silver sulfide is filtered off, the colorless aqueous solution of [2-carboxyquinuclidyl-(3)]-acetic acid is evaporated to dryness in a vacuum. Yield 0.15 g acid with m.p. 265-267°. White crystals, readily soluble in water and dilute mineral acids, insoluble in organic solvents. Yield is 43.8% of theoretical.

b) 3.5 g of [2-carboxyquinuclidyl-(3)]-acetic acid hydrochloride is dissolved at the boil in 350 ml absolute alcohol. The alcoholic solution is filtered from turbidity and treated with 4.3 ml 5.59% alcholic solution of ammonia. On standing for 48 hours, 2.62 g [2-carboxyquinuclidyl-(3)-acetic acid comes down in the form of white plates. M.p. 273°; yield 87.6% of the theoretical.

4.409 mg substance: 9.147 mg CO_2; 2.771 mg H_2O. 4.491 mg substance: 9.312 mg CO_2; 2.892 mg H_2O. 6.744 mg substance: 0.402 ml N_2 (18°, 732 mm). 6.709 mg substance: 0.384 ml N_2 (18°, 732 mm). Found %: C 56.61, 56.59; H 6.91, 7.21; N 6.74, 6.47. $C_{10}H_{15}O_4N$. Calculated %: C 56.34; H 7.04; N 6.57.

Diethyl Ester of [2-Carboxyquinuclidyl-(3)]-acetic Acid.

a) 7 g [2-carboxyquinuclidyl-(3)]-acetic acid hydrochloride and 100 ml purified thionyl chloride are heated on a water bath at 70° for 10 hours. The resultant hydrochloride of the dichloroanhydride of [2-carboxyquinuclidyl-(3)]-acetic acid is insoluble in thionyl chloride. The excess of thionyl chloride is distilled off in vacuum. Its complete removal is effected by twice adding absolute benzene and distilling in vacuum. Into the hydrochloride of the dichloroanhydride is run 140 ml absolute alcohol. The alcoholic solution is heated at the boil for 3 hours, and then the alcohol is driven off in vacuum, the residue treated with 50% potassium carbonate solution, and the separated oil extracted with ether. The ethereal solution is dried with potassium carbonate, then the ether is driven off and the residue distilled in vacuum. 6.25 g diethyl ester of [2-carboxyquinuclidyl-(3)]-acetic acid is obtained with b.p. 126° at 0.3 mm. Yield 82.7% of the theoretical. The compound is a yellow, mobile liquid whose color is not eliminated by repeated distillations. Readily soluble in water and organic solvents; n_D^{20} 1.4797.

6.970 mg substance: 15.949 mg CO_2; 5.281 mg H_2O. 4.400 mg substance: 10.063 mg CO_2; 3.318 mg H_2O. 4.309 mg substance: 1.63 ml 0.01 N H_2SO_4. Found %: C 62.44, 62.41, H 8.47, 8.44; N 5.30. $C_{14}H_{23}O_4N$

b) The diethyl ester of [2-carboxyquinuclidyl-(3)]-acetic acid may be obtained in the form of a colorless liquid by the following method: 15 g [2-carboxyquinuclidyl-(3)]-acetic acid hydrochloride and 150 ml 5% alcoholic solution of hydrogen chloride are heated at the boil until solution is complete (this requires about 6 hours). The alcohol is driven off in vacuum; a fresh addition of 150 ml 5% alcoholic solution is made and heating continued for 4 hours. After removal of the alcohol, the reaction mass is worked up as in a). Vacuum distillation gives the diethyl ester of [2-carboxyquinuclidyl-(3)]-acetic acid in the form of a colorless mobile liquid with b.p. 126° at 0.3 mm; n_D^{20} 1.4797.

Methoiodide of the diethyl ester of [2-carboxyquinuclidyl-(3)]-acetic acid: white, lustrous needles, readily soluble in water and alcohol, insoluble in ether and acetone. M.p. 140-141° (from a mixture of alcohol and ether).

10.666 mg substance: 0.333 ml N_2 (22.5°, 716 mm). 10.298 mg substance: 0.303 ml N_2 (22.5°, 716 mm). 0.1173 g substance: 0.0661 g AgI. Found %: N 3.39, 3.20; I 30.47. $C_{15}H_{26}O_4NI$. Calculated %: N 3.40; I 30.90.

2-Hydroxymethyl-3-(β-hydroxyethyl)-quinuclidine.

A solution of 8.2 g diethyl ester of [2-carboxyquinuclidyl-(3)]-acetic acid in 82 ml absolute ether is added with stirring to a suspension of 4.64 g lithium aluminum hydride in 92 ml ether over a period of 15 minutes, and the reaction mass is heated at the boil for an hour. Addition is then made, while cooling, of 9 ml water; the precipitated lithium and aluminum hydroxides are drained at the pump and thoroughly washed on the filter with chloroform. The combined ethereal and chloroform filtrates are dried with potassium carbonate. Removal of the chloroform and ether leaves 5 g 2-hydroxymethyl-3-(β-hydroxyethyl)-quinuclidine. Yield 88.7% of the theoretical. Colorless, extremely viscous oil, b.p. 156-157° at 0.4 mm. Readily soluble in water and organic solvents.

9.327 mg substance: 0.637 ml N_2 (21°, 718 mm). 5.225 mg substance: 0.353 ml N_2 (18.5°, 728mm). Found %: N 7.49, 7.58. $C_{10}H_{19}O_2N$. Calculated %: N 7.57.

The hydrochloride is obtained by treating an ethereal solution of the compound with an alcoholic solution of hydrogen chloride until the reaction is acid to Congo. White, hygroscopic crystals, readily soluble in water and alcohol, insoluble in ether or chloroform.

2-Chloromethyl-3-(β-chloroethyl)-quinuclidine.

To 5.22 g 2-hydroxymethyl-3-(β-hydroxyethyl)-quinuclidine hydrochloride suspended in 20 ml dry choroform is gradually added 18 ml thionyl chloride while cooling. The homogenous solution is heated at the boil for 30 minutes. The chloroform and excess thionyl chloride are driven off in vacuum and the last traces of thionyl chloride are eliminated by three times adding and distilling off benzene in vacuum. 5.72 g 2-chloromethyl-3-(β-chloroethyl)-quinuclidine hydrochloride is obtained. Yield 94% of the theoretical. White hygroscopic crystals with m.p. 139-140°.

The base is obtained by treating the hydrochloride with 50% potassium carbonate solution and extracting with chloroform. The chloroform extract is dried with potassium carbonate, the chloroform is driven off and the residue distilled in vacuum. B.p. 120-122° at 0.25 mm. Colorless mobile liquid, readily soluble in water and organic solvents.

11.106 mg substance: 4.76 ml 0.01 N H_2SO_4. 4.019 mg substance: 1.73 ml 0.01 N H_2SO_4. Found %: N 6.00, 6.04; $C_{10}H_{17}NCl_2$. Calculated %: N 6.31.

Methoiodide of 2-chloromethyl-3-(β-chloroethyl)-quinuclidine is prepared by running the equivalent amount of methyl iodide into an ethereal solution of the compound. White crystals, readily soluble in water and alcohol, insoluble in ether. M.p. 136°.

12.600 mg substance: 0.421 ml N_2 (20°, 736 mm). 13.700 mg substance: 0.436 ml N_2 (20°, 736 mm). 6.030 mg substance: 10.03 ml 0.01 N $Na_2S_2O_3$. 5.971 mg substance: 9.94 ml 0.01 N $Na_2S_2O_3$. Found %: N 3.77, 3.81; I 35.20, 35.22. $C_{11}H_{20}NCl_2I$. Calculated%: N 3.84; I 34.90.

Di-(diethylaminoethyl) Ester of [2-Carboxyquinuclidyl-(3)]-acetic Acid.

40 ml diethylaminoethanol and the hydrochloride of the dichloroanhydride of [2-carboxyquinuclidyl-(3)]-acetic acid prepared from 3 g of the acid hydrochloride are heated on a water bath at 80-85° for $3\frac{1}{2}$ hours. The excess diethylaminoethanol is then distilled off in vacuum, the residue is treated with 50% potassium carbonate, the separated brown oil is extracted with chloroform. Following the removal of the chloroform, the ester is distilled in vacuum. B.p. 187-189° at 0.3 mm. After a second distillation the substance is obtained in the form of a yellow, mobile liquid, readily soluble in water and organic solvents. Yield 3.42 g or 63% of the theoretical.

3.700 mg substance: 8.661 mg CO_2; 3.282 mg H_2O, 5.529 mg substance: 12.977 mg CO_2; 5.031 mg H_2O. 6.915 mg substance: 5.04 ml 0.01 N H_2SO_4. Found %: C 63.88, 64.05; H 9.92, 10.18; N 10.20. $C_{22}H_{41}O_4N_3$. Calculated %: C 64.23; H 9.98; N 10.22.

Trimethoiodide of di-(diethylaminoethyl) ester of [2-carboxy-quinuclidyl-(3)]-acetic acid is prepared by mixing an alcoholic solution of the compound with methyl iodide. M.p. 197-199° (with decomposition). White crystals, very soluble in water, insoluble in alcohol, ether or acetone.

6.880 mg substance: 2.44 ml 0.01 N H_2SO_4. Found %: N 4.97. $C_{25}H_{50}O_4N_3I_3$. Calculated %: N 5.02.

SUMMARY

1. A method is developed for preparing 2,3-disubstituted quinuclidines starting from the ethyl ester of β-[pyridyl-(4)]-acrylic acid.

2. [2-Carboxyquinuclidyl-(3)]-acetic acid and some if its derivatives and transformation products are synthesized.

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[1] J. Meisenheimer, Ann., 420, 190 (1920); G. Clemo, T. Metcalfe, J. Chem. Soc., 1937, 1989; V. Prelog, Ann., 545, 229 (1940).

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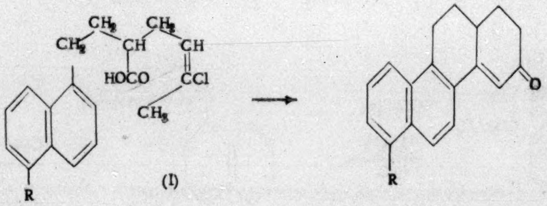
* See Consultants Bureau English translation, page 733 ff.

SYNTHESIS OF POLYNUCLEAR HYDROAROMATIC KETONES

VI. 3-KETO-1,2,3,11,12,12a-HEXAHYDRO-6,7-ACECHRYSENE

S. A. Vardanyan, P. A. Zagorets and G. T. Tatevosyan

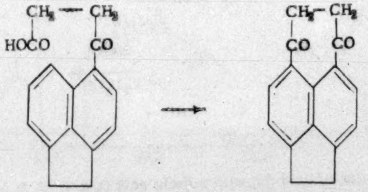
In Communication III [1] it was shown that α-(3-chlorocrotyl)-γ-(1-naphthyl)-butyric acid (I, R = H) is hydrolized by sulfuric acid at the chlorine atom and the resultant keto acid undergoes a double consecutive cyclization into a ketone of the chrysene series:



(I)

The presence of a methoxyl group in the 5-position of the naphthalene nucleus (I, R = CH_3O) which, according to the literature [2] promotes peri-cyclization of the corresponding γ-(1-naphthyl)-butyric acid, dones not in this case hinder the formation of a ketone of the chrysene series [3]; this is evidently due to the presence of a substituent (in the present case the γ-chlorocrotyl radical) in the α-position to the carboxyl group which favors the usual ortho-cyclization of γ-(1-naphthyl)-butyric acids [4].

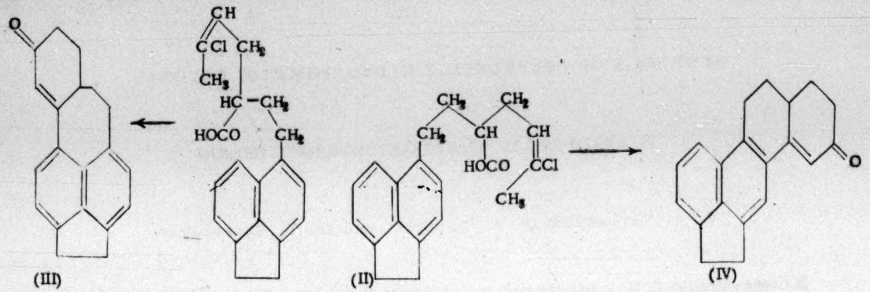
A case of peri-cyclization was described by Fieser and Peters [5] who cyclized β-(3-acenaphthoyl)-propionic acid by fusion with a mixture of aluminum chloride and sodium chloride. The product of cyclization was diketo-dihydro-homophenalene



whose structure was demonstrated by oxidation to naphthalene-1,4,5,8-tetracarboxylic acid. The authors explain the formation of a product of peri-cyclization by the presence in the side chain of a carbonyl group which hinders ortho-cyclization, and by the para-directive influence of the ace-bridge in the nucleus.

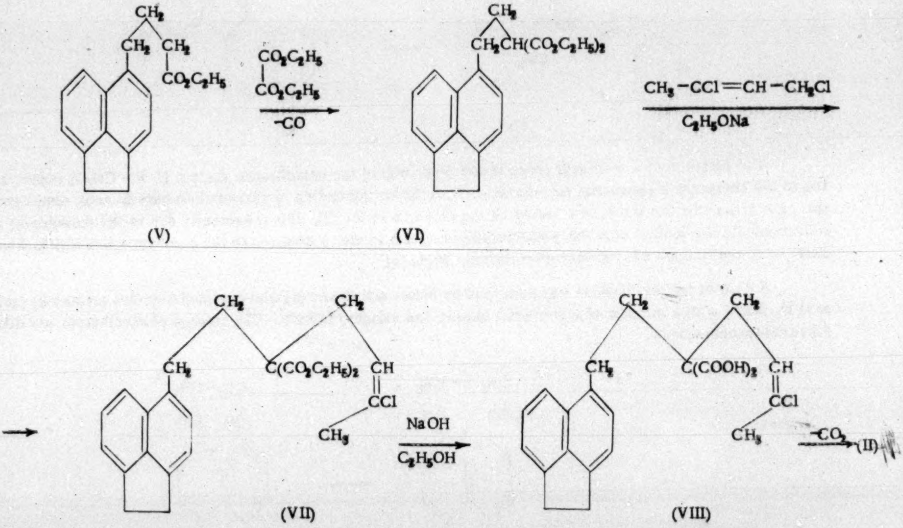
In view of the above considerations, it could be assumed that the effect of sulfuric hydrolysis and cyclization of α-(3-chlorocrotyl)-γ-(3-acenaphthyl)-butyric acid (II) would be the formation, in place of 3-keto-1,2,3,11,12,12a-hexahydro-6,7-acechrysene (IV) or side by side with it, of the isomeric ketone (III) with one seven-membered ring: (See top of next page).

The present communication is devoted to the synthesis of acid (III) and the study of the product of its interaction with sulfuric acid.


CH
CCl
CH$_2$
CH$_3$
HC − CH$_2$
HOCO
CH$_2$
CH$_2$
CH$_2$
CH$_2$
CH
CH
HOCO
CCl
CH$_3$
O
O

(III) (II) (IV)

Acid (II) was synthesized from the ethyl ester of γ-(3-acenaphthyl)-butyric acid previously described by Fieser and Peters [5].


CH$_2$
CH$_2$
CH$_2$
CO$_2$C$_2$H$_5$
CO$_2$C$_2$H$_5$
CO$_2$C$_2$H$_5$
−CO
CH$_2$
CH$_2$CH(CO$_2$C$_2$H$_5$)$_2$
CH$_3$−CCl=CH−CH$_2$Cl
C$_2$H$_5$ONa
CH$_2$
CH$_2$
CH$_2$
C(CO$_2$C$_2$H$_5$)$_2$
CH
CCl
CH$_3$
NaOH
C$_2$H$_5$OH
CH$_2$
CH$_2$
CH$_2$
C(COOH)$_2$
CH
CCl
CH$_3$
−CO$_2$
(II)

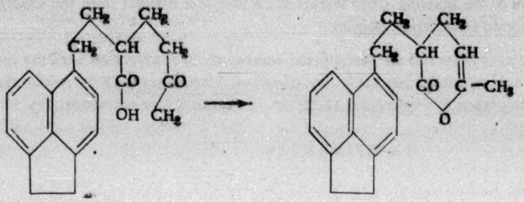
(V) (VI)

(VII) (VIII)

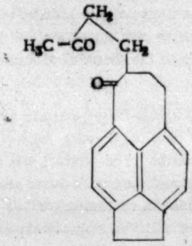
The product of reaction of acid (II) with sulfuric acid (s.g. 1.76) at 50-55° had the composition $C_{20}H_{20}O_2$ and not the composition of the anticipated pentacyclic ketone (III or IV) $C_{20}H_{18}O$. A substance with composition $C_{20}H_{20}O_2$ could be the unsaturated lactone (IX) which could be formed from the product of sulfuric acid hydrolysis (the keto acid) by lactonization followed by dehydration of the lactone: (See top of next page), or it could be one of the diketones (X) and (XI) which could be formed from the same keto acid by intramolecular acylation in the peri- or ortho-position respectively (See next page).

The nature of the compound was elucidated by treating it with boiling aqueous alkali. A salt was not formed as was to be expected in presence of a lactone, but an intramolecular aldol condensation took place with formation of a pentacyclic ketone with the composition $C_{20}H_{18}O$.

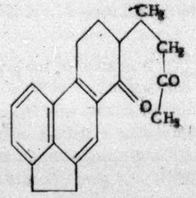
Consequently, contrary to the previously studied cases of sulfuric acid hydrolysis and twofold cyclization of α-(3-chlorocrotyl)-γ-arylbutyric acids, in this case the transformations initiated by sulfuric acid stopped at the stage of formation of the tetracyclic diketone.



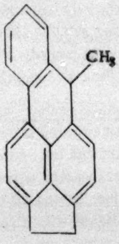
(IX)



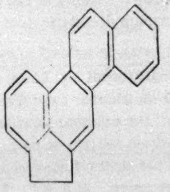
(X)



(XI)



(XII)



(XIII)

In Fig. 1 the ultraviolet absorption curve of ketone $C_{20}H_{18}O$ is compared with the absorption curve of 3-keto-1,2,3,11,12,12a-hexahydrochrysene which was plotted by Wilds and co-workers [6].

The close similarity between the curves is evidence that the investigated ketone is also an α,β-unsaturated ketone with the conjugated double bond system of 1-naphthalacetone (bifurcated maximum at 275-280 mμ), containing the cyclic system of chrysene. The latter fact was confirmed also by study of the product of dehydrogenation of the ketone.

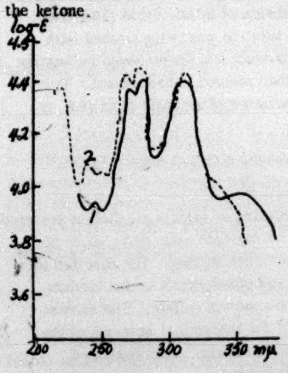


Fig. 1.

1 - Absorption curve of ketone $C_{20}H_{18}O$;

2 - absorption curve of 3-keto-1,2,3,11, 12, 12a-hexahydrochrysene.

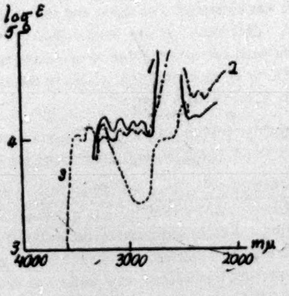


Fig. 2.

1 - Absorption curve of hydrocarbon $C_{20}H_{14}$;

2 - absorption curve of 3-methylchrysene;

3 - absorption curve of benzanthrene.

If the structure of the ketone were to be represented by formula (III), then its dehydrogenation ought to lead to isomerization of the seven-membered ring into a six-membered ring with formation of methyl-acebenzanthrene (XII); another possibility would be complete cleavage of the methyl group with formation of acebenzanthrene. But if the ketone has structure (IV), the product of its dehydrogenation should be 6,7-acechrysene (XIII).

In Figure 2 the absorption curve of the product of dehydrogenation melting at 238-239° and corresponding in composition to formulas (XII) and (XIII) is compared with the absorption curve of 3-methylchrysene, prepared by the action of methyl magnesium iodide on 3-keto-1,2,3,11,12,12a-hydrochrysene followed by dehydrogenation of the product formed. The complete similarity between the curves of both hydrocarbons and their similarity to the absorption curve of chrysene [7], as well as the coincidence of their maxima (318-322, 306-310, 294-296, 283-287 mμ), confirm that these hydrocarbons contain an identical system of condensed aromatic nuclei. Moreover, these curves both in general form and in the position of the maxima differ sharply in an identical manner from the absorption curve of benzanthrene [8] which is plotted in the same diagram.

Consequently, the absorption curves of the investigated compounds in conjunction with the method of preparation and the analytical data demonstrate that the hydrocarbon is 6,7-acechrysene (XIII), while the ketone whose dehydrogenation yields this hydrocarbon is 3-keto-1,2,3,11,12,12a-hexahydro-6,7-acechrysene (IV).

EXPERIMENTAL

The starting β-(3-acenaphthoyl)-propionic acid was prepared as described by Fieser and Peters [5] by condensing succinic anhydride with acenaphthene in presence of aluminum chloride in nitrobenzene solution. The acid was purified from the isomeric β-(1-acenaphthoyl)-propionic acid via the sparingly soluble sodium salt and twice recrystallized. It then melted at 208°. Reduction of 50 g of the keto acid with zinc amalgam and hydrochloric acid, according to the general procedure of Martin [9], gave 30.8 g (65.2% of the theoretical amount) of γ-(3-acenaphthyl)-butyric acid with m.p. 142-143°.

Ethyl ester of γ-(3-acenaphthyl)-butyric acid (V). A mixture of 100 g γ-(3-acenaphthyl)-butyric acid, 500 ml 96% alcohol and 25 ml concentrated sulfuric acid was boiled on the water bath for 6 hours, following which about 200 ml alcohol was driven off and the cooled mixture diluted with 500 ml water. The product was extracted with ether, the ethereal solution was washed with dilute sodium carbonate solution and then with water and dried with anhydrous sodium sulfate. After driving off the ether, distillation of the product in vacuum gave 101.5 g (90.9% of the theoretical) viscous liquid with b.p. 200-202° at 3 mm. The distilled material completely crystallized on standing. M.p. 39°. The ethyl ester of γ-(3-acenaphthyl)-butyric acid was described by Fieser and coworkers [10] as a viscous liquid with b.p. 188° at 0.5 mm.

β-(3-Acenaphthyl)-ethylmalonic ester (VI). To 6.1 g sodium, pulverized in boiling toluene and freed from toluene by washing with dry ether, was added 150 ml absolute ether, followed dropwise by a solution of 12.6 g absolute alcohol in 50 ml dry ether. At the conclusion of the violent reaction, the mixture was boiled on the water bath for 3 hours. To the cooled suspension of alcoholate was then gradually added a solution of 57 g ethyl oxalate in 50 ml absolute ether. Within 30 minutes of the termination of the violent reaction, addition was made to the reaction mixture of a solution of 70 g ester (V) in 100 ml absolute ether. The mixture was gently boiled on the water bath for 20 hours and after cooling it was decomposed by gradual addition of sulfuric acid (15 g conc. acid in 200 ml water). The product was extracted with ether and the ethereal solution was twice washed with water and dried with sodium sulfate. After the ether had been driven off, the product was decomposed by heating in a vacuum of the order of 8-10 mm until the frothing due to evolution of carbon monoxide had ceased. Two distillations in vacuum gave 60 g (67.5% of the theoretical yield) of the monosubstituted malonic ester (VI) in the form of a viscous liquid with b.p. 216-218° at 3 mm.

0.1021 g substance: 0.2776 g CO_2; 0.0668 g H_2O. 0.1102 g substance: 0.3004 g CO_2; 0.0714 g H_2O.
Found %: C 74.15, 74.34; H 7.26, 7.19; $C_{21}H_{24}O_4$. Calculated %: C 74.12; H 7.06.

[β-(3-Acenaphthyl)-ethyl-(3-chloro)-crotyl]-malonic ester (VII). To a solution of sodium alcoholate prepared from 11.75 g sodium and 160 g absolute alcohol was added 170 g monosubstituted malonic ester (VI). After 30 minutes' standing, 75 g freshly distilled 1,3-dichlorobutene-2 was gradually run in with stirring. The reaction mixture was boiled for 6 hours, after which water acidified with hydrochloric acid was added, the reaction product was dissolved in ether, the ethereal solution was washed with water and dried over sodium sulfate. The solvent was driven off and the residue distilled twice in vacuum to give 102 g (47.6% of the theoretical amount) of the disubstituted malonic ester (VII) in the form of a viscous liquid with b.p. 230-232° at 3 mm. It crystallized completely after standing for two days. M.p. 46-47° after recrystallization from alcohol.

0.1194 g substance: 0.0406 g AgCl, 0.1188 g substance: 0.0398 g AgCl. Found %: Cl 8.41, 8.29.
$C_{25}H_{29}O_4Cl$. Calculated %: Cl 8.28.

[β-(3-Acenaphthyl)-ethyl-(3-chloro)-crotyl]-malonic acid (VIII). A mixture of 112 g of the disubstituted malonic ester (VII), 31 g NaOH and 550 ml 90% alcohol was refluxed for 6 hours; 300 ml water was then added and the alcohol distilled off completely. After cooling, the alkaline solution was washed with ether and gently heated on the water bath for complete removal of the ether. Acidification of the cooled solution with dilute hydrochloric acid caused separation of a crystalline substance which melted at 174-175° after recrystallization from benzene. Yield 92.7 g (95.2% of the theoretical amount).

0.1094 g substance: 0.0412 g AgCl. 0.1140 g substance: 0.0430 g AgCl. Found %: Cl 9.34, 9.39. $C_{21}H_{21}O_4Cl$. Calculated %: Cl 9.53.

α-(3-Chlorocrotyl)-γ-(3-acenaphthyl)-butyric acid (II). 90.7 g of the disubstituted malonic acid (VIII) was decarboxylated by heating under reduced pressure. The resultant oil solidified when triturated with methyl alcohol. Recrystallization from alcohol gave 60 g (75% of the theoretical amount) of a colorless crystalline substance with m.p. 114-115°.

0.1024 g substance: 0.0431 g AgCl. 0.1026 g substance: 0.0439 g AgCl. Found %: Cl 10.41, 10.59. $C_{20}H_{21}O_{21}Cl$. Calculated %: Cl 10.80.

1-Keto-2-(γ-ketobutyl)-1,2,3,4-tetrahydro-8,9-acephenanthrene (XI). To 75 g sulfuric acid (s.g. 1.76) was gradually added 10 g of the pulverized substituted butyric acid (II) with stirring. After standing for half an hour, the mixture was heated on a water bath in a carbon dioxide current at 50-55° for 35-40 minutes until acid (II) had dissolved completely. The mass was then left at room temperature for 3 hours, after which period it was poured on to ice. The separated product was dissolved in ether, the ethereal solution washed with dilute caustic alkali, then with water, and dried with sodium sulfate. Removal of the ether left 4.3 g yellow crystals (48.4 % of the theoretical amount on the basis of the formula $C_{20}H_{20}O_2$). M.p. 115-116° after recrystallization from methyl alcohol.

0.0926 g substance: 0.2797 g CO_2; 0.0592 g H_2O. 0.0992 g substance: 0.2980 g CO_2; 0.0612 g H_2O. Found %: C 82.37, 81.92; H 7.10, 6.88. $C_{20}H_{20}O_2$. Calculated %: C 82.19; H 6.85.

In more drastic conditions of treatment with sulfuric acid (higher concentration and temperature and more prolonged heating), the starting substance was almost completely sulfonated.

3-Keto-1,2,3,11,12,12a-hexahydro-6,7-acechrysene (IV). 3 g diketone (XI) was boiled for 4 hours with 40 ml 20% NaOH solution. The substance at first melted, then changed into a solid clot and finally disintegrated into powder. This was filtered, washed with water and twice recrystallized from methyl alcohol (boiling with animal charcoal). Yield 1.9 g (67.6% of the theoretical) of light-yellow, lustrous leaflets with m.p. 184-185°.

0.1012 g substance: 0.3240 g CO_2; 0.0610 g H_2O. Found %: C 87.31; H 6.69. $C_{20}H_{18}O$. Calculated %: C 87.69; H 6.58.

The 2,4-dinitrophenylhydrazone, prepared in an alcoholic medium and recrystallized from chloroform-alcohol mixture, had m.p. 171-172°.

0.1076 g substance: 12.8 ml N_2 (19.5°, 675 mm). Found %: N 12.33. $C_{26}H_{22}O_4N_4$. Calculated %: N 12.33.

6,7-Acechrysene (XIII). 2.5 g ketone (IV) was dehydrogenated with 0.5 g palladized carbon (10% Pd). Dehydrogenation was performed in a gentle stream of CO_2 at 280-300° for 4 hours. The dehydrogenation product was extracted with benzene. Attempts to purify the crude dehydrogenizate (after removal of the benzene) by sublimation were unsuccessful because it decomposed at atmospheric pressure without subliming. It was purified by 3 recrystallizations from benzene-alcohol mixture (boiling with charcoal). Yield 0.5 g crystals with a faint yellow tine, m.p. 238-239°.

0.0906 g substance: 0.3124 g CO_2; 0.0466 g H_2O. Found %: C 94.04; H 5.71. $C_{20}H_{14}$. Calculated %: C 94.44; H 5.56.

3-Methylchrysene was prepared by the method of Wilds and Shunk [11] by the action of magnesium methyl iodide on 3-keto-1,2,3,11,12,12a-hexahydrochrysene [1] followed by dehydrogenation of the unpurified product (m.p. 75-90°) with palladized carbon. Two recrystallizations from benzene-alcohol mixture gave colorless crystals with m.p. 172° (Wilds and Shunk report m.p. 172.5-173.5°).

The orange picrate melted at 165° (the same authors give 166.5-167.5°).

SUMMARY

1. α-(3-Chlorocrotyl)-γ-(3-acenaphthyl)-butyric acid was synthesized and the product of sulfuric acid hydrolysis and cyclization of this acid was investigated.

2. It was shown that, in spite of the presence in the naphthalene nucleus of the starting acid of the 4,5-ace-bridge which favors peri-cyclization of γ-(1-naphthyl)-butyric acids, in the present case ortho-cyclization took place, leading to formation of a compound with the cyclic system of chrysene.

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* See Consultants Bureau English translation, page 293, ff.

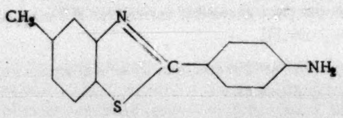
** See Consultants Bureau English translation, page 1349 ff.

IMIDAZOLE DERIVATIVES

VI. SYNTHESIS OF SOME POLYBENZIMIDAZOLES [1]

B. A. Porai-Koshits, L. S. Efros and E. S. Bolchinova

It has been known for a long time that the yellow primuline dyes formed by treatment of p-toluidine with sulfur contain as their main grouping 2-p-aminophenyl-5-methylbenzothizaole (I) (dehydrothio-p-toluidine) and products of its further condensation with sulfur and p-toluidine containing two or even three benzothiazole residues.

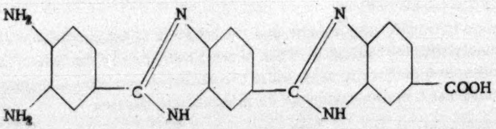


(I)

The thiazole ring [4] is considered to be the chromophoric group of these dyes.

Analogous compounds containing imidazole rings have not hitherto been obtained, and we have therefore undertaken the synthesis of these previously unknown compounds by our previously developed method [5] of condensation of o-diamines with carboxylic acids.

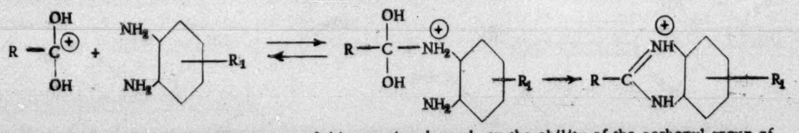
It seemed that the simplest method of preparing these compounds (II) would be polymeric condensation of 3,4-diaminobenzoic acid



(II)

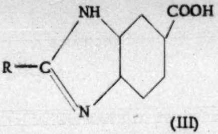
Experiments carried out in this direction, however, showed that 3,4-diaminobenzoic acid is not amenable to the same type of condensation.

The cause of this inability becomes clear from the standpoint of the previously proposed [5] mechanism of condensation of carboxylic acid with an o-diamine in presence of mineral acid:



We see from this scheme that the success of this reaction depends on the ability of the carbonyl group of the carboxylic acid to polarize with formation of an electron deficiency at the carbon atom; this enables the o-diamine to combine at that carbon atom. It is natural that when the radical of the organic acid can compensate for this electron deficiency, the condensation in question proceeds with much greater difficulty. Even the benzene nucleus can exercise such an effect, so that benzoic acid only enters into this reaction in more drastic conditions than an aliphatic acid. In the case of p-aminobenzoic acid, however, conjugation enables the amino group to compensate for this electron deficiency to a considerably larger degree. Therefore, as we established, aminobenzoic acid enters into condensation with o-phenylenediamine very sluggishly, forming the corresponding benzimidazole derivative in a yield of not more that 15% of the theoretical. In regard to the investigated 3,4-diaminobenzoic acid, the unfavorable effect on condensation of the amino group is even more marked than in the case of p-aminobenzoic acid.

Continuing our efforts to obtain the polybenzimidazole derivatives of interest to us, we resolved to weaken the harmful effect of the amino groups in 3,4-diaminobenzoic acid by acetylating them and converting the compound into derivatives of benzimidazole-5-carboxylic acid (III)



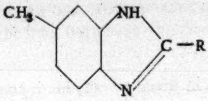
, where: $R=H, CH_3, C_6H_5$.

(III)

Subsequently, however, it was found much more convenient to prepare these compounds not from 3,4-diaminobenzoic acid but by oxidation of the more accessible derivatives of 5-methylbenzimidazole (IV), whose preparation has been described in a previous paper [6].

Our method of oxidation of the methyl groups of these compounds with chromic acid mixture gave close to the quantitative yield of products in all cases.

The theoretical considerations about the ability of acids (III) to condense with o-diamines were fully confirmed. In the very first experiments we obtained compounds with two benzimidazole groupings of the general formula (V)



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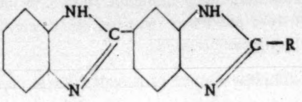
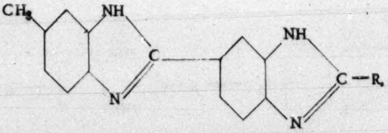


(V)

In this connection it is interesting to note that the behavior of benzimidazole carboxylic acids (III) in this reaction varies profoundly with the radical R. Thus, the most difficult of the investigated compounds to condense is the unsubstituted benzimidazole-5-carboxylic acid, while the easiest to condense is 2-phenylbenzimidazole-5-carboxylic acid, and the acid containing the CH_3 group occupies an intermediate position.

The structure of compounds of the type of (V) was confirmed by their synthesis from 2-diaminophenyl-benzimidazole which was specially prepared; the latter was condensed with organic acids.

For the purpose of further lengthening of the chain, derivatives of benzimidazole-5-carboxylic acid were subjected to condensation with 3,4-toluylenediamine, and the resultant dibenzimidazole compounds, containing a methyl group (VI),



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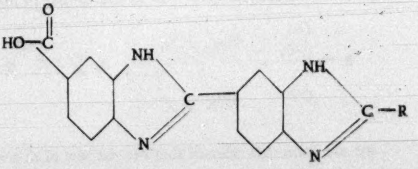
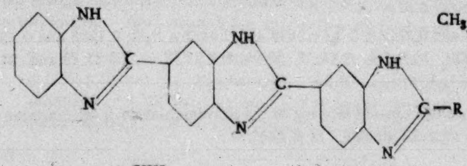


(VII)

were oxidized to the corresponding carboxylic acids (VII).

Their structure was confirmed by decarboxylation to the previously described compounds (V).

Condensation of these acids (VII) with o-phenylenediamine and 3,4-toluylenediamine gave compounds with three benzimidazole rings (VIII) and (IX): (See top of next page.)



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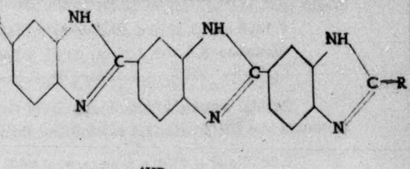

(IX)

In this case the character of the substituent R in the carboxylic acid (VII) naturally did not materially influence the course of the condensation. Due to the poor solubility of these compounds, the chain growth was stopped at this point.

Concerning the general properties of the prepared compounds, as was to be expected, the increasing size of the molecule and the transformation into more complex compounds was accompanied progressively by a fall in solubility and the compounds became more liable to form colloidal solutions; this was especially marked in the case of tribenzimidazole derivatives.

Spectral measurements showed for benzimidazoles an absorption maximum in the region of 2700-2800 A; for dibenzimidazoles one in the region of 3100-3200 A; and for tribenzimidazoles one in the region of 3400-3500 A. As we see, the absorption maximum of these compounds gradually shifts toward the visible region. Visually, however, even tribenzimidazole derivatives are nearly colorless and only exhibit a faint yellow color with a weak intensity. Consequently, in this series we find confirmation of the known theory that imidazole derivatives are less highly colored than thiazoles.

EXPERIMENTAL

Benzimidazole-5-carboxylic Acid.

1.32 g 5-methylbenzimidazole is dissolved in 10 ml sulfuric acid (1:3); with heating to 100-103° and with stirring, dropwise addition is made of 2.4 g chromic acid in 10 ml sulfuric acid of the same concentration as before. 15 minutes after the completion of addition of the oxidizing agent, the reaction mass is cooled with ice water and the precipitated sulfate of benzimidazole-5-carboxylic acid is filtered off. The product is converted to the base by treatment with sodium acetate and is purified by crystallization from water to give 1-1.1 g acid with m.p. 300-325°.

2'-Benzimidazolyl-5-benzimidazole.

1.62 g benzimidazole-5-carboxylic acid, 1.08 g o-phenylenediamine and 10 ml 20% hydrochloric acid are heated in a sealed tube at 180-200° for 4 hours. After cooling, the tube is opened and a considerable residual pressure is manifested (formation of carbon dioxide). The contents of the tube are neutralized with ammonia and the lilac-colored precipitate is filtered and washed with water. The precipitate is then purified in the form of the hydrochloride which is crystallized from concentrated hydrochloric acid. Yield 1.1-1.2 g colorless product with m.p. 362°. The base could not be obtained in the pure form because during crystallization it forms a gelatinous, unfilterable precipitate.

0.1255 and 0.1420 g substance: 0.2508 and 0.2835 g CO_2; 0.0447 and 0.0530 g H_2O. 0.1207 and 0.0964 g substance: 19.9 ml (19°, 755 mm) and 15.4 ml (19°, 757 mm) N_2. 0.1342 and 0.1308 g substance: 10 and 9.8 ml 0.086 N NaOH. Found %: C 54.53, 54.48; H 3.96, 4.17; N 18.3, 18.09; Cl 22.74, 22.87. $C_{14}H_{10}N_4 \cdot 2HCl$. Calculated %: C 54.72; H 3.91; N 18.24; Cl 23.12.

2-Methylbenzimidazole-5-carboxylic Acid.

Oxidation of 2,5-dimethylbenzimidazole to this carboxylic acid with chromic acid in sulfuric acid is carried out as in the previous case. The yield is 70-75% of the theoretical. The acid may be recrystallized from water for complete purification. M.p. 301-302°.

2-Methyl-5-(2'-benzimidazolyl)-benzimidazole.

1.76 g 2-methylbenzimidazole-5-carboxylic acid, 1.08 g o-phenylenediamine and 10 ml 20% hydrochloric acid are heated in a sealed tube for 40 minutes at 180-200°. The reaction mass is neutralized with ammonia, and the reaction product is filtered and crystallized from hydrochloric acid. Yield 2-2.5 g of dihydrochloride in the form of colorless needles with m.p. 339-340°.

0.1368 and 0.1379 g substance: 0.2798 and 0.2823 g CO_2; 0.0578 and 0.0463 g H_2O. 0.1228 and 0.1311 g substance: 8.8 and 9.35 ml 0.086 N NaOH. Found %: C 55.77, 55.83; H 4.70, 3.91; Cl 21.88 and 21.76. $C_{15}H_{12}N_4 \cdot 2HCl$. Calculated %: C 56.07; H 4.36; Cl 22.20.

For the purpose of conversion to the base, the aqueous solution of the dihydrochloride is precipitated with ammonia and the precipitate crystallized from aqueous alcohol. M.p. 340°.

0.1013 and 0.1197 g substance: 0.2693 and 0.2970 g CO_2; 0.0455 and 0.0507 g H_2O. 0.0921 and 0.1174 g substance: 19.2 ml (19°, 742 mm) and 24.9 ml (18°, 748 mm) N_2. Found %: C 72.53, 72.15; H 5.02, 5.07; N 23.13, 21.11. $C_{15}H_{12}N_4$. Calculated %: C 72.56; H 4.84; N 22.58.

Addition of an ammoniacal solution of silver oxide to an alcoholic solution of the compound brings down a flocculent white precipitate of the silver salt of the compound, insoluble in water, alcohol and aqueous ammonia. After drying to constant weight, the silver content was determined by ignition:

1.0466 and 0.5068 g substance: 0.4916 and 0.2338 g Ag. Found %: Ag 46.97, 46.14. $C_{15}H_{10}N_4Ag_2$. Calculated %: Ag 46.72.

The lemon-yellow picrate is precipitated by running together an alcoholic solution of the compound with an alcoholic solution of picric acid. It melts sharply at 282-282.5°. The product contains two molecules of picric acid per molecule of compound:

0.0822 and 0.0857 g substance: 14.5 ml (19°, 735 mm) and 15.2 ml (20°, 753 mm) N_2. Found%: N 19.54, 19.65. $C_{15}H_{12}N_4 \cdot 2C_6H_3N_3O_7$. Calculated %: N 19.83.

2,5'-Dimethyl-5-(2'-benzimidazolyl)-benzimidazole

1.22 g 3,4-toluylenediamine, 1.76 g 2-methylbenzimidazole-5-carboxylic acid and 10 ml 20% hydrochloric acid are heated in a sealed tube for 4 hours at 180-200°. The product is isolated as in the preceding preparation and is purified in the form of the base by crystallization from 50% alcohol. The melting point is high and indefinite.

0.0966 and 0.1620 g substance: 0.2606 and 0.4368 g CO_2; 0.0492 and 0.0824 g H_2O. 0.1036 and 0.1111 g substance: 9.9 ml (18°, 749 mm) and 20.4 ml (19°, 751 mm) N_2. Found %: C 73.60, 73.54; H 5.70, 5.74; N 21.60, 20.85. $C_{16}H_{14}N_4$. Calculated %: C 73.28; H 5.34; N 21.37.

The base is converted to the hydrochloride by crystallization from 20-25% hydrochloric acid. The colorless, fine crystals of the salt melt at above 360°.

0.1795 and 0.1773 g substance: 12.4 and 11.95 ml 0.086 N NaOH. Found %: Cl 21.11, 20.6. $C_{16}H_{14}N_4 \cdot 2HCl$. Calculated %: Cl 21.19.

The bright-yellow picrate comes down immediately on running together alcoholic solutions of the substance and picric acid. M.p. (sharp) 274°.

2-Methyl-5-(5'-carboxy-2'-benzimidazolyl)-benzimidazole

Oxidation of 2,5'-dimethylbenzimidazolyl benzimidazole to the carboxylic acid is performed with chromic acid in the same condition as in preceding preparations. The sulfate of the reaction product is dissolved in aqueous ammonia and treated with hydrochloric acid to bring down the hydrochloride, and the latter is crystallized from 10-15% hydrochloric acid. The colorless hydrochloride melts at about 350°.

0.1489 and 0.1209 g substance: 0.2847 and 0.2304 g CO_2; 0.0555 and 0.0441 g H_2O. 0.1732 and 0.1648 g substance: 22.9 ml (19°, 757 mm) and 22.2 ml (20°, 760 mm) N_2. 0.1170 and 0.1693 g substance: 7.1 and 10.4 ml 0.086 N NaOH. Found %: C 52.18, 52.06; H 4.07, 4.08; N 15.25, 15.23; Cl 19.38, 18.76. $C_{16}H_{12}N_4O_2 \cdot 2\ HCl$. Calculated %: C 52.60; H 3.83; N 15.35; Cl 19.45.

For the purpose of confirming its structure, the acid was decarboxylated. A well-triturated mixture of 0.5 g substance and 3 g soda lime was heated for 10 hours at 280-300°. After solution in water and acidification, the isolated product of reaction was purified by crystallization from aqueous alcohol. The picrate has m.p. 274° and does not give a depression with the picrate of the above-described 2-methyl-benzimidazolyl-benzimidazole.

2-Methyl-5-[2'-benzimidazolyl-5'-(2"-benzimidazolyl)]-benzimidazole

Preparation is performed by condensing 3.7 g of the hydrochloride of the above-described acid with 1 g o-phenylenediamine in 10 ml 15% hydrochloric acid by heating in a sealed tube for 4 hours at 180-200°. The product brought down by treatment of the reaction mass with ammonia is purified by crystallization from dilute hydrochloric acid. Yield about 3.5 g faint-yellow hydrochloride. M.p. above 360°.

0.1486 g and 0.1767 g substance: 0.3002 and 0.3573 g CO_2; 0.0602 and 0.0685 g H_2O. 0.1496 and 0.1582 g substance: 23.6 ml (22°, 765 mm) and 24.8 ml (22°, 764 mm) N_2. 0.1417 and 0.1516 g substance: 10.25 and 11.1 ml 0.086 N NaOH. Found %: C 55.17, 55.1[illegible] H 4.53, 4.33; N 18.17, 18.02; Cl 22.01, 22.35. $C_{22}H_{18}N_6 \cdot 3HCl$. Calculated %: C 55.75; H 4.01; N 17.74; Cl 22.49.

2,5'-Dimethyl-5-[2'-benzimidazolyl-5'-(2"-benzimidazolyl)]-benzimidazole

The product was prepared similarly to the preceding preparation by condensation of the acid with 3,4-toluylenediamine and was purified by crystallization from dilute hydrochloric acid. Yield 85-90% of the theoretical. M.p. about 400°.

0.1168 and 0.1332 g substance: 0.2416 and 0.2741 g CO_2; 0.0480 and 0.0544 g H_2O. 0.1414 and 0.1511 g substance: 21.2 ml (21°, 766 mm) and 22.5 ml (22°, 768 mm) N_2. 0.1060 and 0.1431 g substance: 7.5 and 10.1 ml 0.086 N NaOH. Found %: C 56.44, 56.15; H 4.59, 4.57; N 17.34, 17.14; Cl 21.60, 21.54. $C_{23}H_{18}N_6 \cdot 3HCl$. Calculated %: C 56.59; H 4.31; N 17.23; Cl 21.84.

2-Phenylbenzimidazole-5-carboxylic Acid

15 g 2-phenyl-5-methylbenzimidazole is dissolved in 300 ml concentrated sulfuric acid and the solution gradually diluted with 600 ml water. Into the boiling solution is gradually run a solution of 18 g chromic acid in 30 ml water. A violent reaction takes place, at the conclusion of which the sulfate of the carboxylic acid crystallizes out from the still-boiling solution. The reaction mass is cooled and diluted with 600 ml water, the product is filtered and washed with water. It is purified by reprecipitation with hydrochloric acid from the ammoniacal solution and by crystallization from dilute hydrochloric acid. Yield 16 g hydrochloride of the carboxylic acid. Long, colorless needles (from dilute hydrochloric acid) m.p. 304-305°. The acid is readily soluble in dilute ammonia and in sodium carbonate solution; it is precipitated from solution by hydrochloric and sulfuric acids, and less readily by acetic acid, in the form of the respective salts.

The hydrochloride of this compound was subjected to potentiometric titration with the glass electrode; for this purpose 0.1500 g was dissolved in 12 ml 0.1 N caustic alkali and titrated with 0.1 N hydrochloric acid. Two potential jumps were obtained, the first corresponding to the instant of absence of free alkali from the solution after addition of 0.75 ml 0.1 N hydrochloric acid (pH 8.4) and the second (weaker) corresponding to the appearance in the solution of free hydrochloric acid after addition of 6.4 ml 0.1 N hydrochloric acid.

Found: according to the first point: (12 ml − 0.75 ml = 11.25 ml); equivalent weight = 133.3; according to the first and second points: (6.4 ml − 0.75 ml = 5.65 ml); mol. wt. 267. $C_{14}H_{10}O_2N_2 \cdot HCl$. Calculated: mol. wt. 274.5; equiv. wt. 137.25.

0.1084 g substance: 9.4 ml N_2 (15°, 766 mm). 0.1495 g substance: 5.5 ml 0.1 N solution $AgNO_3$. Found %: N 10.34; Cl 13.06. $C_{14}H_{10}O_2N_2 \cdot HCl$. Calculated %: N 10.20; Cl 12.95.

2-Phenyl-5-(2'-benzimidazolyl)-benzimidazole

2.75 g 2-phenylbenzimidazole-5-carboxylic acid hydrochloride and 1.5 g o-phenylenediamine are heated in a sealed tube with 10 ml 15% hydrochloric acid for 6 hours at 180-200°. The precipitate is filtered and twice treated with ammonia solution while hot to remove traces of carboxylic acid. The product is purified by several crystallizations from dilute hydrochloric acid; during this operation addition is made to the first hot crystallization solution of a very small amount of chromic acid solution to decompose the blue dye formed by a secondary reaction. Yield 3 g. Fine colorless needles (from dilute hydrochloric acid) with m.p. 323-326°. The product is soluble on heating in dilute hydrochloric acid and is salted out by an excess of it.

The free base is obtained by treating the hydrochloride with ammonia; it crystallizes from aqueous alcohol in fine, white needles. M.p. 308-310°. The base is insoluble in dilute acetic acid.

Analysis of the base:

0.1024 g substance: 0.2910 g CO_2, 0.0425 g H_2O. 0.0655 g substance: 10 ml N_2 (12°, 762 mm). Found %: C 77.37; H 4.62; N 18.30. $C_{20}H_{14}N_4$. Calculated %: C 77.42; H 4.52; N 18.05.

Analysis of the hydrochloride:

0.0752 g substance: 10.5 ml N_2 (18°, 760 mm). 0.1003 g substance: 2.85 ml 0.1 N solution $AgNO_3$.
Found %: N 16.33; Cl 10.10. $C_{20}H_{15}N_4Cl$. Calculated %: N 16.15 ; Cl 10.25.

2-Phenyl-5-(5'-methyl-2'-benzimidazolyl)-benzimidazole

5 g 2-phenylbenzimidazole-5-carboxylic acid hydrochloride and 3.7 g 3,4-toluylenediamine are heated in a sealed tube with 20 ml 15% hydrochloric acid for 6 hours at 180-200°. The product is worked up and purified in the same way as the preceding preparation. Yield 4.7 g. Fine, colorless needles (from dilute hydrochloric acid), m.p. 311-315°.

The free base crystallizes from aqueous alcohol in fine needles with m.p. 329-331°. The base is insoluble in dilute acetic acid.

Analysis of the base:

0.1051 g substance: 0.2971 g CO_2 and 0.0473 g H_2O. 0.0832 g substance: 12.1 ml N_2 (14°, 764 mm).
Found %: C 77.80; H 5.04. N 17.48. $C_{21}H_{16}N_4$. Calculated %: C 77.78; H 4.93; N 17.27.

Analysis of the hydrochloride:

0.1505 g substance: 4.1 ml 0.1 N solution $AgNO_3$. Found %: Cl 9.68. $C_{21}H_{17}N_4Cl$. Calculated %: Cl 9.83.

2-Phenyl-5-(5'-carboxy-2'-benzimidazolyl)-benzimidazole

4 g 2-phenyl-5-(5'-methyl-2'-benzimidazolyl)-benzimidazole is dissolved in 160 ml concentrated sulfuric acid and the solution is gradually diluted with 240 ml water. Into the boiling solution is gradually run a solution of 2.8 g chromic acid in 10 ml water. At the conclusion of the reaction, the sulfate of the carboxylic acid crystallizes from the still-boiling solution The reaction mass is cooled and diluted with 500 ml water; the product is filtered off and well washed with water.

The product is purified by three reprecipitations with hydrochloric acid from hot ammoniacal or sodium carbonate solution and thoroughly washed with water. Yield 3.5-4 g of the hydrochloride of the carboxylic acid.

Fine, barely yellow needles with m.p. 314-319°. The acid dissolves with heating in dilute ammonia and sodium carbonate solution and is brought down by hydrochloric, sulfuric and acetic acids. The salt of the acid is readily isolated from solution by adding sodium chloride solution. Soluble in alcohol.

0.1500 g acid was dissolved in 12 ml 0.1 N caustic alkali and subjected to potentiometric titration with 0.1 N hydrochloric acid using a glass electrode. Two potential jumps were obtained, the first corresponding to the instant of titration of the excess alkali after addition of 4.2 ml hydrochloric acid (pH 8.8) and the second corresponding to the appearance of free hydrochloric acid after addition of 8 ml 0.1 N hydrochloric acid.

Found: according to the first point: (12 ml−4.2 ml = 7.8 ml); equiv. wt. 192.3; according to the first and second points: (8 ml−4.2 ml = 3.8 ml); mol. wt. 395. $C_{21}H_{14}O_2N_4 \cdot HCl$. Calculated: mol. wt. 390.5; equiv. wt. 185.25.

0.0985 g substance: 12 ml N_2 (18°, 760 mm). Found %: N 14.36. $C_{21}H_{15}O_2N_4Cl$. Calculated %: N 14.34.

2-Phenyl-5-[2'-benzimidazolyl-5'-(2"-benzimidazolyl)]-benzimidazole

1.5 g 2-phenyl-5-(5'-carboxy-2'-benzimidazolyl)-benzimidazole and 0.75 g o-phenylenediamine are heated with 10 ml 10% hydrochloric acid in a sealed tube at 200-220° for 10 hours. The precipitate is filtered, washed with water, and twice treated with sodium carbonate solution with heating for removal of residues of carboxylic acid. The product is purified by dissolving in dilute acetic acid and precipitating as the dihydrochloride by addition to the hot solution of concentrated hydrochloric acid. The purification is repeated several times. The first time a few drops of chromic acid solution are added with the hydrochloric acid to decompose the dye. Yield 1.2 g. Barely yellowish, slender, long needles of hydrochloride, darkening slightly but not melting even at 360°. Almost insoluble in water and organic solvents.

0.2021 g substance: 30.0 ml N_2 (18°, 742 mm); 0.1500 g substance: 6.0 ml 0.1 N solution $AgNO_3$.
Found %: N 16.88; Cl 14.15. $C_{27}H_{18}N_6 \cdot 2HCl$. Calculated %: N 16.80; Cl 14.20.

2-Phenyl-5-[2'-benzimidazolyl-5'-(5"-methyl-2"-benzimidazolyl)]-benzimidazole

3 g 2-phenyl-5-(5'-carboxy-2'-benzimidazolyl)-benzimidazole and 1.5 g 3,4-toluylenediamine are heated with 20 ml 10% hydrochloric acid in a sealed tube at 200-220° for 16-20 hours. The product is separated and purified as

above. Yield 1.8 g. The barely yellow, slender, long needles of the dihydrochloride darken, but do not melt even at 360°. Almost insoluble in water and organic solvents.

The base is obtained by treatment of the salt with ammonia. It is likewise nearly insoluble in organic solvents but dissolves readily in aqueous acetic acid to form a salt, and it may be isolated from solution by adding hydrochloric acid or even sodium chloride solution.

0.0610 g substance: 8.2 ml N_2 (16°, 770 mm). 0.1002 g substance: 0.0557 g AgCl. 0.1500 g substance: 5.6 ml 0.1 N $AgNO_3$. Found %: N 16.1; Cl 13.6, 13.7. $C_{28}H_{20}N_6 \cdot 2HCl$. Calculated %: N 16.4; Cl 13.8.

Experiments on Condensation of 3,4-Diaminobenzoic Acid

2.25 g 3,4-diaminobenzoic acid hydrochloride is heated with 10 ml 20% hydrochloric acid in a sealed tube at 180-200° for 40 minutes. A fairly high pressure was always present in the tubes after completion of the reaction. The contents of the tubes are filtered and the solid crystallized several times from 10% hydrochloric acid. Yield 0.1 g, m.p. 325-330°. The yield increases slightly if 1 g o-phenylenediamine is added to the tube before the reaction.

The resultant 3,4-diaminophenylbenzimidazole absorbs nitrous acid without forming a diazo compound. In acetic acid solution it gives with phenanthrenequinone a copious green precipitate with the characteristic reactions for phenanthrazines.

For confirmation of its structure, the product was condensed with formic acid and with acetic acid. 1 g product and 0.5 ml acid were heated in 5 ml 20% hydrochloric acid at 180-200° for 40 minutes. The resultant compound, containing two benzimidazole groupings, were purified in the form of the hydrochlorides and found to be identical with these previously described derivatives in respect to melting points and the melting points of their picrates (no depression in mixed melting tests).

SUMMARY

1. Products of a new and previously undescribed type — linearly arranged polybenzimidazole derivatives — may be prepared by various routes, of which the best is condensation of a carboxylic acid with o-toluylenediamine followed by oxidation of the methyl group of the formed imidazole derivative to carboxyl and further condensation with an aromatic o-diamine. By this method substances are obtained containing two and three benzimidazole groupings in a line.

2. The prepared compounds, compared with the known primuline dyes containing similarly arranged benzothiazole rings, have not so deep a color.

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* See Consultants Bureau English translation, page 725 ff.

** See Consultants Bureau English translation, page 1555.

IMIDAZOLE DERIVATIVES

VII. PREPARATION OF BENZIMIDAZOLE SULFONIC ACIDS BY THE SINTERING METHOD [1]

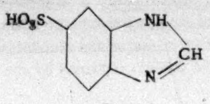
L. S. Efros

Treatment of benzimidazole derivatives with concentrated sulfuric acids gives the corresponding sulfonic acids which, according to the literature [2], may be used as emulsifying agents.

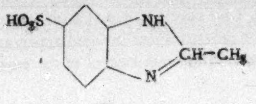
We have succeeded in also preparing the sulfonic acids of these compounds by another method, which consists in the sintering of their acid sulfates. Hitherto, this method was known only for the preparation of sulfonic acids of mainly aromatic amines and has never been applied for the introduction of the sulfo group into heterocyclic systems.

In the present case, as well as generally in processes of sintering, during heating of the sulfates of benzimidazole derivatives at above the melting point, water is first evolved and sulfamic acids are apparently formed which are easily hydrolyzed by water. Consequently, if the melt is poured into water after completion of this stage of the reaction, the original benzimidazole can be very easily isolated by neutralization. On further heating of the melt, however, these intermediate products are smoothly transformed into the usual sulfonic acids.

By this method we obtained good yields of the sulfonic acids of benzimidazole (I) and 2-methylbenzimidazole (II):



(I)



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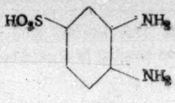

(III)

The position of the sulfo group in them was confirmed by their synthesis by the condensation of 1,2-phenylenediamine-4-sulfonic acid (III) with formic and acetic acids by the previously described method [3].

In passing from the above benzimidazole derivatives to compounds with more complex substituents in the 2-position, the sintering reaction is very seriously hindered, the yields fall, and the preparation of sulfonic acids from them by the sinter method no longer presents practical value.

As was shown earlier [4], there are specific features about the chemical behavior of benzimidazole and its derivatives which can only be explained on the basis of the structure of the molecule of these compounds as a whole. Moreover, the reaction under consideration reveals the close relation between these compounds and aromatic amines of the benzene series.

EXPERIMENTAL

Benzimidazole-5-sulfonic Acid

Preparation by the method of sintering of benzimidazole sulfate. The sulfate is prepared from 11.8 g base with m.p. 170° (0.1 mole) which is thoroughly triturated in a mortar with 6 ml concentrated sulfuric acid (s.g. 1.84) (0.12 mole). The initially hot liquid mass rapidly solidifies. It is transferred to a porcelain funnel and well washed with ether at the pump. After drying, about 19 g crystalline benzimidazole sulfate is obtained.

0.1081 and 0.1075 g substance: 0.1173 and 0.1175 g $BaSO_4$. Found %: H_2SO_4 45.6, 45.8.
$C_7H_6N_2 \cdot N_2SO_4$. Calculated %: H_2SO_4 45.3.

5 g of the so prepared benzimidazole sulfate is placed in a short test tube of maximum width and heated on an oil bath at 220-240° until water vapor ceases to come off. The bath temperature is thereupon raised to 260-280° and heating continued until a specimen of the melt when dissolved in water no longer deposits benzimidazole when ammonia is added. The melt is crystallized from a very small amount of water to give 4-4.5 g

benzimidazole-5-sulfonic acid in the form of colorless needles with m.p. 365-367° (after 3-4 crystallizations). The product is readily soluble in aqueous ammonia and soda, less soluble in water, and poorly soluble in alcohol.

0.0988 and 0.1005 g substance: 12.0 and 12.3 ml N_2 (18°, 758 mm). 0.1220 g substance: 0.1467 g $BaSO_4$. Found %: N 14.20, 14.32; S 16.50. $C_7H_6O_3N_2S$. Calculated %: N 14.13; S 16.15.

Preparation by condensation of 1,2-phenylenediamine-4-sulfonic acid with formic acid. 1.12 g phenylenediamine-sulfonic acid (0.005 mole), 1 ml formic acid and 5 ml water are heated in a sealed tube at 180-190° for 40 minutes. After cooling, the tube is opened and the crystals are filtered. Yield 0.95 g. After several crystallizations from a small amount of water, the product is obtained as needles with m.p. 365-367°. A mixed sample with the sulfonic acid prepared as above melts at the same temperature.

2-Methylbenzimidazole-5-Sulfonic Acid

Preparation by sintering of 2-methylbenzimidazole sulfate. The sulfate was prepared in the same way as benzimidazole sulfate.

0.1173 and 0.1137 g substance: 10.1 and 9.9 ml 0.1 N NaOH. Found %: H_2SO_4 42.2, 42.7. $C_8H_8N_2 \cdot H_2SO_4$. Calculated %: H_2SO_4 42.6.

Sintering of this sulfate is effected as in the preceding case, except that a longer period is required and the temperature has to be raised to 280-290°. The yield of 2-methylbenzimidazole-5-sulfonic acid is 2-2.5 g from 5 g salt (about 50% of the theoretical). The substance forms colorless needles, very soluble in hot water, less soluble in cold water and insoluble in alcohol. The m.p. is very high and indefinite.

0.1012 and 0.1025 g substance: 11.5 and 11.7 ml N_2 (18°, 758 mm). 0.1597 g substance: 0.1712 g $BaSO_4$. Found %: N 13.3, 13.35; S 14.70. $C_8H_8O_3N_2S$. Calculated %: N 13.26; S 15.08.

Preparation by condensation of 1,2-phenylenediamine-4-sulfonic acid with acetic acid. 1.12 g phenylenediamine-sulfonic acid (0.005 mole), 1 ml acetic acid and 5 ml water are heated in a sealed tube at 180-190° for 40 minutes. This reaction gave 1 g of a product whose outward appearance, solubility in water and alcohol and behavior on heating in a capillary were entirely reminiscent of the properties of the product obtained by the sinter method.

0.1461 g substance: 0.1597 g $BaSO_4$. Found %: S 14.98. $C_8H_8O_3N_2S$. Calculated %: S 15.08.

SUMMARY

The method of sintering of sulfates of benzimidazole and 2-methylbenzimidazole was applied to the preparation of the sulfonic acids of these compounds, thus demonstrating the possibility of application of this method also to the synthesis of sulfonic acids of certain heterocyclic compounds.

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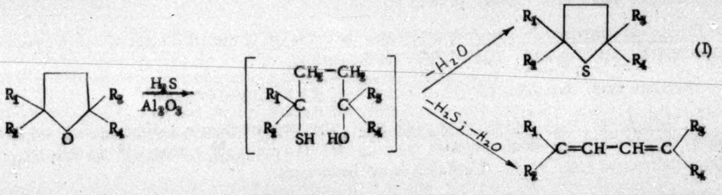
TRANSFORMATION OF 3,3-DIMETHYLTETRAHYDROFURAN INTO 3,3-DIMETHYLTETRAHYDROTHIOPHENE AND 3,3-DIMETHYLPYRROLIDINE. XL.

Yu. K. Yuryev, G. Ya. Kondratyeva and N. K. Sadovaya

In a previous investigation it was shown that homologs of tetrahydrofuran, in the conditions of catalytic transformation of oxygenated heterocycles into rings with other heteroatoms, are transformed –depending on the number, magnitude and position of the methyl groups in the ring–either into the corresponding homologs of tetrahydrothiophene or into diene hydrocarbons or into a mixture of both compounds.

2,2,5,5-Tetraalkyltetrahydrofurans only gave a mixture of diene hydrocarbons with various positions of the double bonds in presence of alumina in a hydrogen sulfide atmosphere [1]. When 2,2-dimethyltetrahydrofuran was led over the catalyst in the same conditions, two competing reactions took place simultaneously: dehydration of the oxygen-containing heterocycle with formation of unsaturated hydrocarbons and transformation into 2,2-dimethyltetrahydrothiophene.

It is clear that the usual reaction of replacement of the bridge oxygen by another heteroatom is suppressed in the case of 2,2-disubstituted tetrahydrofurans. Dialkyltetrahydrofurans with another structure, namely 2,5-dimethyltetrahydrfuran [2] and 2,4-dimethyltetrahydrofuran [3], react normally and are transformed in good yield into 2,5- and 2,4-dimethyltetrahydrothiophene, respectively. The first stage in the transformation of oxygen-containing heterocycles into sulfur-containing ones (rupture of the ring at the carbon-oxygen linkage) with addition of the elements of hydrogen sulfide undoubtedly proceeds identically in all compounds of the tetrahydrofuran series, but the direction of the subsequent dehydration of the intermediately formed 1,4-mercaptooxy compound is determined by the peculiarities of its structure.



In the case of formation of ditertiary 1,4-mercaptooxy compounds from 2,2,5,5-tetraalkyltetrahydrofurans, the process takes place exclusively according to scheme (II), i.e., with simultaneous cleavage of water and hydrogen sulfide, and leads to diene hydrocarbons. In the case of primary-tertiary 1,4-mercaptoalcohols (R_1=R_2=H), the reaction proceeds simultaneously in the two possible directions (I) and (II), and gives a mixture of dienes (products of dehydration and hydrogen sulfide cleavage) and the corresponding tetrahydrothiophene homolog. Finally, disecondary (R_2=R_4=H) and primary-secondary (R_2=R_3=R_4=H) 1,4-mercaptooxy compounds –like diprimary ones (formed from tetrahydrofuran in which R_1=R_2=R_3=R_4=H) –normally undergo dehydration to tetrahydrothiophene homologs.

Alkyl radicals located at the β-carbon atom of tetrahydrofuran excercise the least influence on the yield of the corresponding tetrahydrothiophene homolog, and 3-alkyltetrahydrofurans are transformed into 3-alkyltetrahydrothiophenes only with slightly lower yields than tetrahydrofuran itself: 3-methyltetrahydrofuran gives 3-methyltetrahydrothiophene in a yield of 80% [4], while tetrahydrothiophene is obtained from tetrahydrofuran in a yield of 90% [5]. Attention is also drawn to the fact that 3-alkyltetrahydrothiophenes are formed from 3-alkyltetrahydrofurans in better yields than are the corresponding α-alkyltetrahydrothiophenes from α-alkyltetrahydrofurans [6].

The transformation of tetrahydrofuran homologs into pyrrolidine homologs is marked by the same regularities, but the yield of pyrrolidine homologs is lower than the yield of their sulfur-containing analogs.

In this investigation we examined the transformation of 3,3-dimethyltetrahydrofuran into the corresponding nitrogen- and sulfur-containing heterocyclic compounds. It was established that the presence of two methyl radicals at one and the same carbon atom of the ring did not hinder the transformation of 3,3-dimethyltetrahydrofuran into 3,3-dimethyltetrahydrothiophene (yield 73%) and into 3,3-dimethylpyrrolidine (yield 41%).

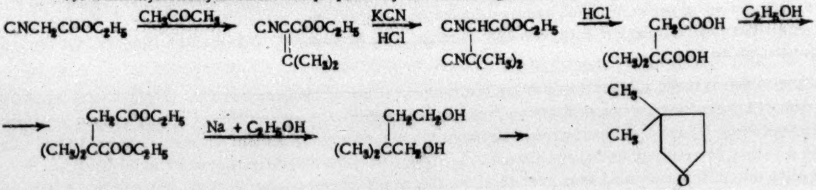
Regarding 3,3-dimethyltetrahydrofuran itself, we must note that the literature contains erroneous statements. In describing the reduction of the diethyl ester of α,α-dimethylsuccinic acid with sodium in ethyl alcohol, Blanc [6] reported that he isolated from the reaction mixture a few milliliters of a substance with b.p. 85° which did not mix with water and possessed an acetone-like odor. Blanc suggested that this substance was 3,3-dimethyltetrahydrofuran, although the data of the elementary analysis deviated considerably from those calculated for 3,3-dimethyltetrahydrofuran.

After preparing 3,3-dimethyltetrahydrofuran in the pure state, we were convinced that Blanc's suggestion was erroneous; the constants and properties of 3,3-dimethyltetrahydrofuran are entirely different from those of the substance isolated by Blanc.

EXPERIMENTAL

1. Preparation of 3,3-Dimethyltetrahydrofuran

3,3-Dimethyltetrahydrofuran was prepared by the following series of reactions:



a) Ethyl ester of α,β-dicyano-β-methylbutyric acid [7]: b.p. 152-156° (22 mm); n_D^{20} 1.4382; d_4^{20} 1.0486; MR_D 45.13. $C_9H_{12}O_2N_2$. Calculated MR_D 45.05.

Literature data: b.p. 136-141° (9 mm) [7].

b) α,α-Dimethylsuccinic acid was prepared by hydrolysis of the ethyl ester of α,β-dicyano-β-methylbutyric acid [7]: b.p. 139-140°. Yield 75% of the theoretical.

Literature data: b.p. 138-139° [7]; b.p. 141-142° [8]; b.p. 139-140° [9].

c) Diethyl ester of α,α-dimethylsuccinic acid was prepared from α,α-dimethylsuccinic acid and absolute alcohol by saturation with hydrogen chloride [10]; b.p. 101° (15 mm); n_D^{20} 1.4233; d_4^{20} 0.9936; MR_D 51.84. $C_{10}H_{18}O_4$. Calculated MR_D 51.69. Yield 62% of the theoretical.

Literature data: b.p. 101° (15 mm) [8]; b.p. 215°; n_D^{20} 1.421; d_4^{20} 0.994 [11].

d) 2,2-Dimethylbutanediol-1,4 was prepared by reduction of the diethyl ester of α,α-dimethylsuccinic acid with sodium in absolute alcohol [12]: b.p. 117° (8 mm); n_D^{20} 1.4513; d_4^{20} 0.9739; MR_D 32.63. $C_6H_{14}O_2$. Calculated MR_D 32.96. Yield 63% of the theoretical.

Literature data: b.p. 123° (9 mm); d_0^4 0.996 [12].

e) 3,3-Dimethyltetrahydrofuran. A mixture of 9.2 g 2,2-dimethylbutanediol-1,4 and 0.9 g finely triturated aluminosilicate catalyst was heated in a distillation flask at 180-190°. The distillate was saturated with potassium carbonate and the 3,3-dimethyltetrahydrofuran (which floated to the surface) was dried with calcium chloride and distilled through a column. Two distillations over sodium gave pure 3,3-dimethyltetrahydrofuran with b.p. 98-99° (750 mm); n_D^{20} 1.4121; d_4^{20} 0.8455; MR_D 29.44. $C_6H_{12}O$. Calculated MR_D 29.35.

Found %: C 71.28, 71.46; H 12.15, 12.12. $C_6H_{12}O$. Calculated %: C 71.99; H 12.09. Yield 95% of the theoretical. 3,3-Dimethyltetrahydrofuran has not been described in the literature.

2. Transformation of 3,3-Dimethyltetrahydrofuran into 3,3-Dimethyltetrahydrothiophene

10.5 g 3,3-dimethyltetrahydrofuran was passed over alumina in a stream of hydrogen sulfide at 350° with a velocity of 10 drops/min. The catalyzate was collected in a well-cooled receiver and was saturated with solid KOH and extracted with ether. After driving off the ether, the reaction product was distilled through a column to give a fraction with b.p. 143-146° (755 mm). After a second distillation over sodium, the 3,3-dimethyltetrahydrothiophene possessed the following constants: b.p. 144-145° (755 mm); n_D^{20} 1.4861; d_4^{20} 0.9374; MR_D 35.55. $C_6H_{12}S$. Calculated MR_D 35.40. The melting point of the $HgCl_2$ compound is 148°.

Found %: C 61.98, 62.01; H 10.30, 10.21; S 27.60, 27.59. $C_6H_{12}S$. Calculated %: C 62.05; H 10.35; S 27.59.

Yield 8.9 g (73% of the theoretical). 3,3-Dimethylthiophane has not been described in the literature.

3. Transformation of 3,3-Dimethyltetrahydrofuran into 3,3-Dimethylpyrrolidine

10.2 g 3,3-dimethyltetrahydrofuran was passed over activated Al_2O_3 in a stream of ammonia at 325° with a velocity of 6 drops/min. The catalyzate was saturated with solid NaOH and extracted with ether. The ether extract was dried with KOH, the ether was driven off and the residue distilled through a column. The first distillation gave a fraction with b.p. 100-110°. After a second distillation the 3,3-dimethylpyrrolidine had the constants: b.p. 110-111° (760 mm); n_D^{20} 1.4386; d_4^{20} 0.8422; MR_D 30.95. $C_6H_{13}N$. Calculated MR_D 31.31. Yield 4.2 g (41% of the theoretical).

The picrate (recrystallized from alcohol) had m.p. 158°.

Found %: N 17.51. $C_{12}H_{17}O_7N_4$. Calculated %: N 17.57.

3,3-Dimethylpyrrolidine has not been described in the literature.

SUMMARY

1. The 3,3-dimethyltetrahydrofuran described in this paper differs considerably from the substance erroneously assumed by Blanc to be 3,3-dimethyltetrahydrofuran.

2. It was established that 3,3-dimethyltetrahydrofuran is smoothly transformed into 3,3-dimethyltetrahydrothiophene in the conditions of catalytic transformation of oxygen-containing heterocycles into rings containing other heteroatoms.

3. By means of the indicated reaction, 3,3-dimethyltetrahydrofuran is also transformed into 3,3-dimethylpyrrolidine.

4. It was established that when two methyl groups are present at one and the same carbon atom in the β-position of the tetrahydrofuran ring, the catalytic transformation of the oxygen-containing heterocycle only proceeds in the direction of formation of cyclic systems with other heteroatoms.

5. The introduction of a second methyl group in the β-position of the tetrahydrofuran ring has considerably less influence on the yield of nitrogen- and sulfur-containing products of catalytic transformation of heterocycles than the introduction of the first methyl group.

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* See Consultants Bureau English translation, page 405 ff.

** See Consultants Bureau English translation, page 577 ff.

*** See Consultants Bureau English translation, page. 697 ff.

D

THE ACTION OF AROMATIC DIAZO COMPOUNDS ON COMPOUNDS OF THE TYPE OF ALKYLACETOACETIC ESTERS AS A METHOD OF PREPARATION OF ARYLHYDRAZINES OF KETO ACIDS, α-AMINO ACIDS AND NITROGEN-CONTAINING HETEROCYCLIC COMPOUNDS

XV. SYNTHESIS OF D,L-GLUTAMIC ACID

V. V. Feofilaktov and N. K. Semenova

Glutamic acid was first isolated from the hydrolyzate of vegetable protein by Ritthausen [1], who also proposed for it the structural formula which was later confirmed by Dittmar [2], Markovnikov [3] and Wolff. The latter effected its synthesis [4]. A series of synthetic methods for its preparation are known and may be divided broadly into four groups: those based on reduction of α-nitrosoglutaric acid or its esters, prepared by various routes; synthesis using α-ketoglutaric acid; syntheses by the Strecker-Zelinsky method; and syntheses on the basis of amino-malonic ester.

Wolff [4] was the first to prepare glutamic acid from the nitrosoglutaric acid derived from levulinic acid. This synthesis is only of historical interest. McIlwain and Richardson [5] obtained nitrosoglutaric acid from α-acetoglutaric ester, which, in turn, was prepared from α-chloropropionic and acetoacetic esters by a slight modification of the method of Clemo and Welch [6]; they prepared glutamic acid from nitrosoglutaric acid in a yield of 39% reckoned on the original chloropropionic ester; Hamlin and Hartung [7] raised the yield by the same method to 74% by conducting the reduction in presence of platinum oxide at a hydrogen pressure of 10 atmospheres, and thereby rendered this method suitable for preparative purposes.

The difficultly accessible α-ketoglutaric acid is the starting material in several methods [8, 9] which are devoid of preparative value. In the same class are also the syntheses of Keimatsu and Sugasawa [10, 11] by the Strecker-Zelinsky method from β-formylpropionic acid and its esters which are derived from acrolein.

Alkylation of aminomalonic ester with β-chloropropionic ester did not give a high yield of glutamic acid; the yields could be considerably improved, however, by alkylating benzaminomalonic ester with β-bromopropionic ester, and this method is suitable for preparative purposes [13].

Acetaminomalonic ester was alkylated with acrylonitrile [14] or with methacrylonitrile [15]; subsequent hydrolysis and decarboxylation gave glutamic acid in good yields. Phthaliminomalonic ester was alkylated [16] with β-chloropropionic ester or with methyl acrylate; hydrolysis (requiring drastic conditions) and decarboxylation of the intermediate products gave glutamic acid in good yields.

Of the syntheses described, the simplest is the one utilizing the relatively accessible α-acetoglutaric ester. There are difficulties, however, in connection with its nitrosation with alkyl nitrite or nitrosylsulfuric acid to form hydroximinoglutaric ester and in connection with the subsequent reduction by the methods of McIlwain and Hamlin, resulting in low yields or requiring special apparatus. It was therefore a matter of interest to synthesize this amino acid from α-acetoglutaric ester by the relatively simple method of one of us: the synthesis through the stage of the readily accessible arylhydrazones of α-keto acids which enables the above difficulties to be avoided.

On submitting the o-tolyhydrazone of α-ketoglutaric acid * to reduction with zinc dust and acetic acid, we did indeed obtain glutamic acid with a yield at this stage of 81-87%. The synthesis stages may be represented by the following scheme: (see page 888).

The accessibility of the starting material (I), the high yield of the intermediate o-tolylhydrazone (II) which did not require purification, the simplicity of isolation of the free amino acid (III) from the reaction mixture and its formation in high yield are advantages of this method of synthesis of glutamic acid.

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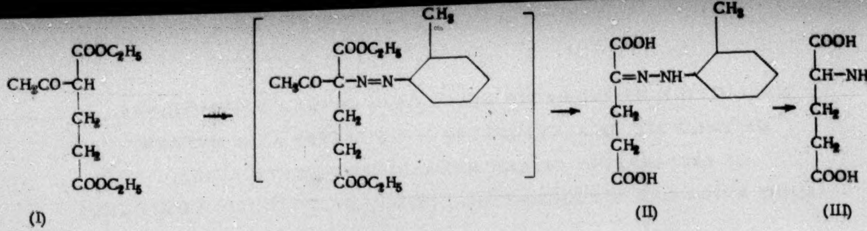
* The o-tolylhydrazone had a series of advantages over the phenylhydrazone from the preparative angle.



EXPERIMENTAL

D,L-Glutamic acid (III). A solution of 5.0 g of the o-tolylhydrazone of α-ketoglutaric acid (m.p. 159-160°) [18], in 50 ml. conc. acetic acid was placed in a long-necked 200 ml round-bottomed flask and heated on a boiling water bath; to this solution was added zinc dust (16 g) in small portions, each portion being dissolved before the next was added; after a period of 20-30 minutes from the start of heating, a total of 50 ml water was introduced in small portions over a period of 1½ - 2 hours. Reduction by heating on the water bath required a period of about 4 hours (negative Bülow reaction). The solution was filtered and the zinc dust on the filter was repeatedly washed with hot water; the filtrate was diluted with water and extracted several times with ether to eliminate the o-toluidine. Zinc ion was precipitated with hydrogen sulfide, the precipitate of zinc sulfide was repeatedly washed on the filter with hot water, and the filtrate and the wash waters evaporated to dryness on a water bath in vacuum. The residue was a thick, light-brown mass which crystallized when stirred with a small quantity of absolute alcohol; the crystals of glutamic acid were drained at the pump, washed with absolute alcohol and dried; weight 2.38-2.55 g; yield 81-87%; m.p. 185-189° with decomposition. Recrystallization from 70% alcohol gave D,L-glutamic acid in the form of colorless, rhombic or hexagonal tablets melting at 195-196° (uncorr.) with decomposition. Literature data: 197° [17], 198° [4].

Found %: N 9.76, 9.76. $C_5H_9O_4N$. Calculated %: N 9.52.

SUMMARY

The possibility was shown of extending V. V. Feofilaktov's method for preparation of α-aminocarboxylic acids to α-aminodicarboxylic acids.

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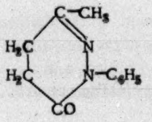
ACTION OF AROMATIC DIAZO COMPOUNDS ON COMPOUNDS OF THE TYPE OF ALKYLACETOACETIC ESTERS AS A METHOD OF PREPARATION OF ARYLHYDRAZONES OF α-KETO ACIDS, α-AMINO ACIDS AND NITROGEN-CONTAINING HETEROCYCLIC COMPOUNDS

XVI. 1-ARYL-PYRIDAZONE-3-CARBOXYLIC ACIDS AND PRODUCTS OF THEIR TRANSFORMATION

V. V. Feofilaktov and N. K. Semenova

Pyridazone and its derivatives have been relatively little investigated. Their discovery and initial investigation were associated with the clarification of the chemical nature and transformations of hydrazones of ketocarboxylic acids and pyrazolones. Thus, E. Fischer discovered the ability of levulinic acid phenylhydrazone to lose water with formation of a new compound (I) which he called the anhydride of levulinic acid phenylhydrazone [1].



(I)

A little later [2,3] a number of transformations of this compound was studied.

The chemical nature of this anhydride was finally established by investigations [4,5] undertaken in connection with the study of pyrazolones. It was established that reaction of esters of β-ketocarboxylic acids with hydrazine and its derivatives leads to pyrazolone derivatives; in the case, however, of γ-keto acids and their derivatives, such a reaction leads to formation of six-membered nitrogen heterocycles in the shape of pyridazone derivatives [4]. Thus, for example, the product of condensation of hydrazine hydrate with benzoylacetic ester is pyrazolone, while that with the ester of β-benzoylpropionic acid is pyridazone.

Condensation of other γ-ketocarboxylic acids and their esters [4] gave respectively carboxy- and carbethoxypyridazone derivatives and products of their transformation and pyridazone itself.

On the basis of a study of the behavior of benzopyridazones on alkylation and acetylation, the conclusion was reached [5,6] that tautomerism between the CO and NH groups existed in the pyridazones. Unlike pyrazolones, however, pyridazones do not enter into the azo-coupling reaction.

In general, these two groups of compounds differ markedly from each other also in respect to other chemical properties. Thus, pyrazolone derivatives are known to be stable to acids and alkalies but decompose when distilled; pyridazone derivatives, in contrast, are modified by acids and alkalies and distil without decomposition.

When 1-phenylpyridazone-3-carboxylic acid was subjected to the action of an alcoholic solution of hydrogen chloride, it did not give the expected ester of this acid since the pyridazone ring was ruptured and reclosure to the pyrrole ring took place with formation of an indole derivative — the ethyl ester of 2-carbethoxyindolyl-3-acetic acid [7].

Wolff observed rupture of the pyridazone ring in an alkaline medium: on subjecting 3-methylpyridazone to the action of sodium ethylate, he obtained valeric acid [8].

Pyridazones differ from pyrazolones in being relatively easily oxidized, and advantage was taken of this property in the synthesis of derivatives of phenylpyridazone, phthalazine [9] and pyridazine [10].

In recent years no systematic study has been made of the pyridazones. The literature contains only isolated references to new representatives of this class which were prepared mainly for the purpose of identification of derivatives of γ-ketocarboxylic acids [11, 12, 13] or of substituted hydrazines [14,15].

Interest in pyridazone derivatives has recently increased somewhat due to their application to the synthesis of sulfanilamide derivatives of pyridazone and pyridazine [15], which exhibit a high bacteriostatic activity and possess chemotherapeutic interest. Thus, for example, 6-sulfanilamido-3-methylpyridazine, prepared from 3-methylpyridazone, manifested a higher bacteriostatic activity than sulfathiazole [16].

In our opinion, one of the causes of the neglect of the study of these interesting pyridazone derivatives is the absence of a simple method for their preparation: the only known method of synthesis starts from hydrazones and difficultly accessible keto acids; no attempts had been made to replace the latter by more accessible starting materials.

Bearing in mind the similarity in the methods of preparation of pyrazolones and pyridazones and starting from the ability (discovered and investigated by one of us) of acetosuccinic ester to couple with aryldiazoniums to directly give pyrazolone derivatives [17], we decided to investigate the applicability of this reaction to the preparation of pyridazone derivatives; for this purpose α-acetosuccinic ester was replaced by α-acetoglutaric ester.

We used various aryldiazoniums in the azo-coupling reaction. However, as we had previously observed [18], pyridazone derivatives are not directly formed in the process of azo-coupling, and the coupling products are azo esters or arylhydrazones of esters of α-ketoglutaric acid, saponification of which yields the corresponding arylhydrazones of α-ketoglutaric acid.

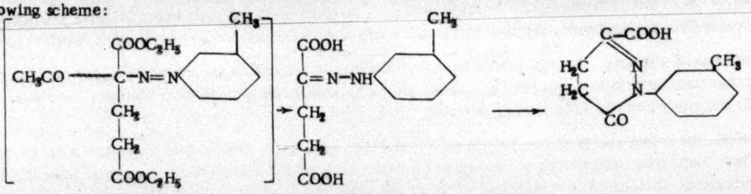
An attempt was therefore made to prepare pyridazones from the separated arylhydrazones. On investigating the ability of these arylhydrazones to undergo ring-closure to pyridazones, it was established that even when subjected to the action of acids (dilute sulfuric, hydrochloric, acetic) or acetic anhydride or when heated, they showed little tendency to be transformed into pyridazone derivatives.

Thus, out of twelve arylhydrazones of α-ketoglutaric acid [18], only two (phenyl- and m-tolylhydrazones) could be cyclized to pyridazones by heating with dilute acids.

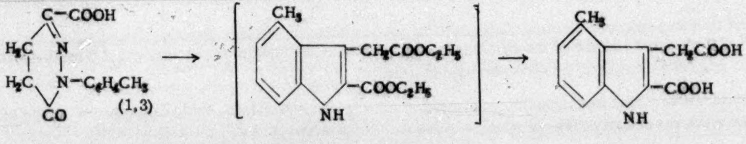
The ability of the m-tolylhydrazone to transform into 1-(m-tolyl)-pyridazone-3-carboxylic acid is apparently due to the CH_3 group — with a weak o,p-orienting effect — being in the m-position to the =N—NH— group and not exerting any appreciable influence on the latter, in consequence of which the latter behaves like the =N—NH— group of an unsubstituted phenylhydrazone.

It should be noted that the γ-phenyl- and γ-m-tolylhydrazones of β-pyruvyl-propionic acid, unlike the phenyl- and m-tolylhydrazones of α-ketoglutaric acid, do not undergo cyclization to pyridazones in spite of the similarity of their structures. It is possible that this is bound up with participation of the hydrogen of the —NH-group in the formation of a hydrogen bond at the carbonyl of the acetyl group which hinders its participation in the cleavage of water, i.e. in the closure of the pyridazone ring.

A study of two of the pyridazone derivatives that we prepared revealed that one of them was identical with the 1-phenylpyridazone-3-carboxylic acid previously described by Wislicenus [7]. We could not find a description of the second derivative — 1-(m-tolyl)-pyridazone-3-carboxylic acid — in the literature; its formation may be represented by the following scheme:



1-Phenylpyridazone-3-carboxylic acid was reduced to glutamic acid and reconverted into the original phenylhydrazone of α-ketoglutaric acid. Both of the pyridazone-carboxylic acids were transformed into the corresponding indole derivatives.



EXPERIMENTAL

1-Phenylpyridazone-3-carboxylic Acid

2.36 g α-Ketoglutaric acid phenylhydrazone (m.p. 152-153°) [18] was heated on a gauze with 40 ml 3% hydrochloric acid until completely dissolved (10-15 minutes). The cooled solution deposited lustrous, slightly pink crystals of 1-phenylpyridazone-3-carboxylic acid in the amount of 2.0 g (91.7%), melting at 169-170°. After recrystallization from water (with addition of carbon), the colorless, lamellar crystals melted at 172°.

Found %: N 12.70, 12.65. $C_{11}H_{10}O_3N_2$. Calculated %: N 12.84.

Literature data [7]: m.p. 172°.

For the purpose of hydrolysis, 2.18 g 1-phenylpyridazone-3-carboxylic acid was dissolved in 40 ml 10% NaOH and boiled on a gauze for 3-5 minutes. The cooled solution was diluted with water and carefully acidified with conc. hydrochloric acid. The precipitated crystals, consisting of the original phenylhydrazone of α-ketoglutaric acid, weighed 2.32 g (98.6 %) after drying and melted at 152-153° (from alcohol); the composition of the phenylhydrazone was confirmed by a mixed melting test and by determination of the equivalent. Found equiv. 119; 120. $C_{11}H_{12}O_4N_2$. Calculated equiv. 118.

Reduction of 2.18 g 1-phenylpyridazone-3-carboxylic acid with zinc dust and acetic acid in the conditions described in the preceding communication [20] gave D, L-glutamic acid: 0.33 g, i.e. 22%.

For conversion into the indole derivative, 1-phenylpyridazone-3-carboxylic acid and 5 times the amount of absolute ethyl alcohol were refluxed in a flask on a water bath; dry hydrogen chloride was led in through the condenser. Heating was accompanied by deposition of crystals of ammonium chloride on the sides of the flask and was continued for 30 minutes. On cooling, the liquid was poured on to ice-water mixture. The resultant colorless crystals were separated, washed with water and dried. After recrystallization from aqueous ethyl alcohol, the ethyl ester of 2-carbethoxyindolyl-3-acetic acid melted at 85-86° in agreement with the literature [7, 19]; yield quantitative.

A mixed sample with the preparation obtained from α-ketoglutaric acid phenylhydrazone did not give a depression.

Found %: N 4.91, 4.82. $C_{15}H_{17}O_4N$. Calculated %: N 5.09.

1-(m-Tolyl)-pyridazone-3-carboxylic Acid

2.5 g α-Ketoglutaric acid m-tolylhydrazone (m.p. 149°) was digested with 40 ml 5% aqueous sulfuric acid until dissolved. The solution was filtered hot; on cooling with ice, colorless crystals (2.14 g or 92.2%) were deposited; m.p. 146-147°. The crystals did not give a Bulow reaction and had excellent solubility in ethyl and methyl alcohols, ethyl acetate, ether and hot water. After two recrystallizations from aqueous ethyl alcohol, the colorless, lustrous needles of 1-(m-tolyl)-pyridazone-3-carboxylic acid melted at 152°.

Found %: N 12.08, 12.24; equiv. 231, 229. $C_{12}H_{12}O_3N_2$. Calculated %: N 12.07; equiv. 232.

A mixed test with the preparation from the diethyl ester of α-carbethoxyglutaric acid and m-toluidine [18] did not give a melting point depression.

4-Methyl-2-carboxyindolyl-3-acetic Acid

2.32 g 1-(m-tolyl)-pyridazone-3-carboxylic acid (m.p. 152°) and 10 ml 10% alcoholic solution of sulfuric acid were refluxed on a water bath. Two hours after the commencement of heating, there was appreciable separation of ammonium sulfate crystals; heating was continued for 8 hours.

The reaction mixture — a light-brown liquid — was poured into water which contained ice; the resultant viscous oil was separated from the alcoholic liquid by decantation and saponified with 10% alcoholic-aqueous solution of NaOH. Acidification of the aqueous solution of the salt caused greyish crystals of acid to separate in the amount of 1.97 g (84.4%). The substance is readily soluble in acetone, ethyl acetate, ether, methyl and ethyl alcohols and glacial acetic acid; very sparingly soluble in benzene.

After recrystallization from aqueous ethyl alcohol with addition of carbon, 4-methyl-2-carboxyindolyl-3-acetic acid formed colorless crystals which melted at 186° with decomposition.

Found %: N 5.93, 5.78; equiv., 109, 113. $C_{12}H_{11}O_4N$. Calculated %: N 6.00; equiv. 116.5.

SUMMARY

1. It was established that arylhydrazones of α-ketoglutaric acid and arylhydrazones of β-pyruvylpropionic acid do not spontaneously cyclize to the pyridazone ring.

2. Arylhydrazones of α-ketoglutaric acid differ in respect of ease of cyclization into pyridazone derivatives; it was only possible to cyclize the phenyl- and m-tolylhydrazones.

3. γ-Arylhydrazones of β-pyruvylpropionic acid generally do not cyclize to pyridazone derivatives in the conditions investigated.

4. The possibility is demonstrated of reduction of 1-phenylpyridazone-3-carboxylic acid into D,L-glutamic acid

4. The possibility is demonstrated of reduction of 1-phenylpyridazone-3-carboxylic acid into D,L-glutamic acid and of transformation into the original α-ketoglutaric acid phenylhydrazone, and of transformation into 2-carboxyindolyl-3-acetic acid in quantitative yield.

5. 1-(m-Tolyl)-pyridazone-3-carboxylic acid was also transformed into 4-methyl-2-carboxyindolyl-3-acetic acid in high yield.

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** See Consultants Bureau English translation, page 887 ff.

N-ARYL AMIDES OF HYDROXY CARBOXYLIC ACIDS AND THEIR TRANSFORMATION INTO HETEROCYCLIC COMPOUNDS

XX. REGULARITIES OF INTRAMOLECULAR CYCLIZATION IN ARYL AMIDES OF HYDROXY CARBOXYLIC ACIDS

P. A. Petyunin and V. S. Shklyaev

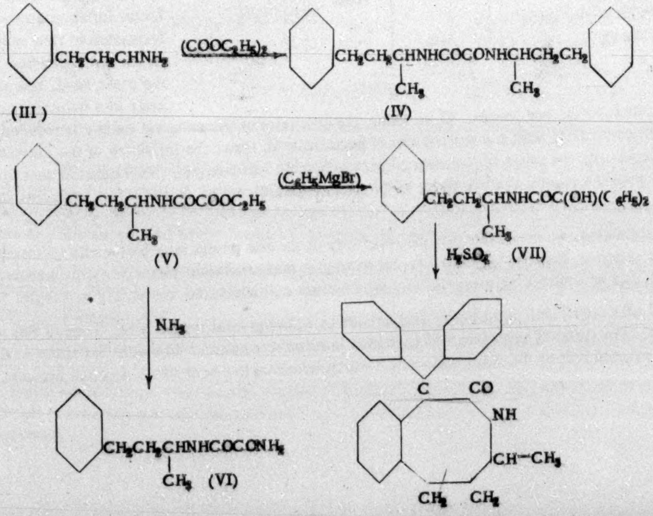
Many investigations have been devoted to the problem of formation of cyclic systems from open-chain compounds. At the present time the ideas of Mohr [1] and Ruzicka [2] are generally accepted. These authors consider that ring closure is determined by two factors acting simultaneously: the strain in the formed ring and the distance between the reacting groups. Isolation of the molecule, as one of the conditions of cyclization, may be achieved by using dilute solutions in high vacuum [3]. These concepts, however, do not cover all the diverse causes influencing the process of ring formation. N. A. Domnin [4] points out that with a minimum of six, if not five, members in the ring, the reluctance to cyclize is due not to strain but to other factors such as spatial separation of the end reactive groups. There are probably other causes (still unknown). Study of the regularities of formation of ring systems from open-ring compounds have been made for the most part with carbon rings.

According to very recent experimental data, the valence angles of trivalent nitrogen and of oxygen in organic compounds only differ slightly from the angles of a regular tetrahedron [5]. Consequently the process of ring formation ought to be studied to an equal extent with reference to heterocycles. We decided to study the regularities of formation of ring systems during intramolecular condensation of aryl amides of hydroxy carboxylic acids. In previous investigations it had been established that intramolecular ring closure is possible in aryl amides of two types of hydroxycarboxylic acids:

$ArNHCO(CH_2)_nC(OH)Ar_2$ (I) and $Ar(CH_2)_nNHCOC(OH)Ar_2$ (II).

Compound (I), when $n = 0$ or 1, forms 5- or 6-membered rings, respectively. When $n = 2$, the hetero-ring does not close and saponification occurs with formation of an aromatic amine and a γ-hydroxy carboxylic acid [6]. Compounds (II) are more useful because their structure imparts exceptional resistance to saponification [6]. Successful condensations of this type were performed with $n = 0$, 1 and 2 [7].

We set ourselves the objective of performing the reaction for $n = 3$ and of forming an 8-membered ring. The latter was synthesized by the following scheme:



Heating of 1-phenyl-3-aminobutane (III) with ethyl oxalate gave two compounds: the di-(1-phenyl-3-butylamide) of oxalic acid (IV) and the ethyl ester of 1-phenyl-3-butyloxamic acid (V) (expt. 1). The latter was converted into the amide (VI) (expt.2). Treatment of (V) with phenyl magnesium bromide gave the 1-phenyl-3-butylamide of benzilic acid (VII), which underwent intramolecular condensation to the lactam of 2-(γ-aminobutyl)-triphenylacetic acid (VIII) (expt. 4).

To clarify the problem of our investigation, the starting substances taken were compounds of the type of $\mathrm{ArCH_{2n}NHCOC(OH)Ar'_2}$, where n = 0, 1, 2 and 3; Ar' = $\mathrm{C_6H_5-}$, $\mathrm{p\text{-}CH_3C_6H_4-}$ and $\mathrm{p\text{-}CH_3OC_6H_4}$. A new series of compounds was prepared in this way (expts. 5, 6, 7). The velocity of ring closure in these was determined by the procedure described in detail in the preceding communication.

The relation between the velocity of ring closure and the distance separating the reacting groups was clarified with reference to the formation of 5-, 6-, 7- and 8-membered rings. The data obtained are set forth in Table 1 (aryl amides nos. 1, 2, 3 and 4). The reactivity of the carbonyl carbon atom in these aryl amides was substantially identical since it is governed by the nature of the radical attached to them. These compounds have the same basicity (they form halochromic salts with 88% $\mathrm{H_2SO_4}$ and their transformation into heterocyclic compounds requires an identical amount of sulfuric acid). Consequently, the differences in the speeds of ring closure may be explained by the spatial separation of the end reactive groups.

We see from the data that with increasing distance between the end reactive groups, the speed of ring closure decreases in the order: 5>6>7>8, i.e. a reciprocal dependence exists between the speed of closure of a ring and its size. This conclusion is fully consistent with the literature data for polymethylene rings [8] and cyclic imines [9]. On comparing these data, however, with the velocity of ring closure in p-tolylic acid anilide (aryl amide No. 5), we see that the stated relation between size of ring and ease of cyclization is far from possessing general validity. Thus, the 5-membered heterocycle in aryl amide no. 5 closes 27 times slower than the 6-membered ring (aryl amide no. 2), 20 times slower than the 7-membered ring (aryl amide no. 3), and 5 times slower than the 8-membered ring (aryl amide no. 4).

TABLE 1

Velocity of Closure of 5-, 6-, 7- and 8-Membered Rings in Aryl Amides of α-Hydroxycarboxylic Acids *

Prep. No.	Formula	Amount of $\mathrm{H_2SO_4}$ (ml)	Velocity of closure of ring at 20°	Size of ring
1	$\mathrm{C_6H_5NHCOC(OH)(C_6H_5)_2}$	5	400	5
2	$\mathrm{C_6H_5CH(CH_3)NHCOC(OH)(C_6H_5)_2}$	5	328	6
3	$\mathrm{C_6H_5CH_2CH_2NHCOC(OH)(C_6H_5)_2}$	5	240	7
4	$\mathrm{C_6H_5CH_2CH_2CH(CH_3)NHCOC(OH)(C_6H_5)_2}$ . .	5	60	8
5	$\mathrm{C_6H_5NHCOC(OH)(C_6H_4CH_3\text{-}p)_2}$	1.5	12	5

The high velocity of formation of 6-, 7- and 8-membered ring systems in aryl amides of benzilic acid in comparison with the 5-membered ring of p-tolylic acid anilide can no longer be explained by the spatial separation of the end groups as the sole factor influencing the formation of ring systems which are strain-free. On the other hand, this anomaly can be readily explained by the differing reactivities of the end groups. As we know, the reactivity of the carbonyl carbon is reduced in the anilide of p-tolylic acid, in comparison with the aryl amides of benzilic acid, under the influence of the electron-donating methyl groups. Consequently, the speed of ring closure is considerably reduced [10]. This signifies that, apart from the distance between the reacting groups, the reactivity of the groups themselves is a factor in the formation of cyclic systems.

On the basis of the literature data, we may infer that the reactivity of the end groups may profoundly influence the ease of formation of cyclic systems. Ruczika [11] observes, for example, that maximum yields of cyclic ketones from salts of dicarboxylic acids can be attained by using thorium salts but not calcium salts. According to Ziegler [12],

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* Experiments were performed with 0.015 mol. solutions of aryl amides in 1 liter glacial acetic acid. 1 ml of this solution was used in an experiment. The speed of ring closure is expressed in relative numbers. The unit was taken as the velocity of closure of the 5-membered ring of the o-anisidide of 4,4'-dimethoxybenzilic acid which was 300 minutes.

replacement of lithium by potassium improves the reaction results in the cyclization of dicarboxylic acid nitriles. Freundlich and Salomon [9] established that the introduction of a phenyl group in the α-position of a ω-haloalkylamine increases the reaction velocity more than 1000 times. There are, however, no studies in the literature of a comprehensive character on the relation between reactivity of end groups and formation of cyclic systems. This fact becomes understandable when we bear in mind that in the compounds used by the cited authors for formation of rings, the reactivity of the groups varied within narrow limits.

The distance factor has the greatest influence on cyclization when the reactivity of the end groups is reduced. Thus, for example, in aryl amides of p-tolylic acid (Table 2) the 5-membered ring closes 3.1 times as fast as the 6-membered ring; while in aryl amides of benzilic acid (aryl amides 1 and 2, Table 1), whose end groups are more reactive, the 5-membered ring is formed 1.2 times as fast as the 6-membered ring.

TABLE 2

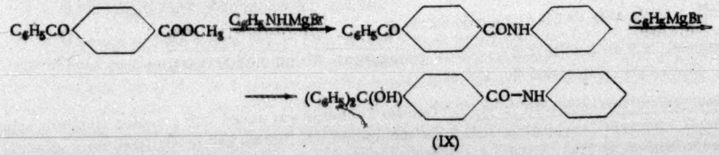
Velocity of Closure of 5- and 6-Membered Rings in Aryl Amides of p-Tolylic Acid

Prep. No.	Formula	Amount of H_2SO_4 (ml)	Velocity of closure of ring at 30°	Size of ring
1	$C_6H_5NHCOC(OH)(C_6H_4CH_3\text{-}p)_2$	1.5	43	5
2	$C_6H_5CH(CH_3)NHCOC(OH)(C_6H_4CH_3\text{-}p)_2$.	1.5	13.6	6

In the course of this research it was a matter of interest to study ring closure in the compounds $Ar(CH_2)_nNHCOC(OH)(C_6H_4OCH_3\text{-}p)_2$, where n = 0, 1, 2, because they contain less reactive groups than aryl amides of p-tolylic acid. From the data of Table 3 we see that ring closure is very slow in the 5-membered heterocycle (aryl amide no. 1) while aryl amides 2 and 3 are generally not transformed into cyclic compounds (expt. 8).

In connection with the effect of the terminal reactive groups on ring closure, we must revise our ideas about the limits of condensation in the sense of the magnitude of the formed ring. Experiments have shown that in compounds $Ar(CH_2)_nNHCOC(OH)(C_6H_5)_2$ condensation is possible when n = 3 with formation of an 8-membered ring, whereas in the compounds $Ar(CH_2)_nNHCOC(OH)(C_6H_4OCH_3\text{-}p)_2$ condensation only proceeds when n = 0 with formation of a 5-membered ring. Consequently the limits of cyclization of aryl amides of α-hydroxy carboxylic acids may be broadened by introducing electron-accepting groups into the phenyl radicals at the carbonyl carbon atom, and the limits may be narrowed by introducing electron-donating substituents.

Ring closure is of theoretical interest in the case of aryl amides in which a strain factor is involved apart from the distance factor. From this standpoint we synthesized the anilide of p-triphenylcarbinol carboxylic acid (IX) according to the scheme below (expts. 9 and 10).



(IX)

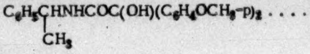
We unsuccessfully attempted to realize the intramolecular closure of the heterocycle in (IX) (expt. 11). Inspection of the formula of molecule (IX) indicated that an exceptionally large deformation of the valence angles of the carbon atoms would be required for approach of the carbonyl carbon to the o- or p-position of the aryl amide residue to a distance equal to the length of the covalent bond.

A problem that inevitably arises in the study of cyclic systems relates to the reactions competing with ring formation. Reactions of formation of monomeric ring systems are known to be accompanied by the formation of polymeric compounds [13].

Repeated experiments on condensation of aryl amides of hydroxy carboxylic acids established that the reactions give high yields of only monomeric cyclic systems. The absence of products of intermolecular reaction is due to the intramolecular ring closure in aryl amides of hydroxy carboxylic acids proceeding in a cation of a halochromic salt. In this connection not only are intermolecular reaction between ions of identical charge hindered but also their close approach.

Hence for organic compounds capable of ring closure by an ionic mechanism, neither dilution nor a vacuum is necessary for isolation of the molecule, since the presence of a charge definitely ensures isolation.

TABLE 3

Prep. No.	Formula	Amount of H_2SO_4 (ml)	Velocity of ring closure at 20°	Size of ring
1	o-$CH_3OC_6H_4NHCOC(OH)(C_6H_4OCH_3\text{-}p)_2$.	0.1	1	5
2	 $C_6H_5CH(CH_3)NHCOC(OH)(C_6H_4OCH_3\text{-}p)_2$	0.1	Does not cyclize	6
3	$C_6H_5CH_2CH_2NHCOC(OH)(C_6H_4OCH_3\text{-}p)_2$.	0.1	Does not cyclize	7

We unsuccessfully attempted to realize the intermolecular reaction of aryl amides with phenols according to the following scheme:

$$ArNHCOC(OH)Ar_2 + C_6H_5OH \rightarrow H_2O + ArNHCOC(C_6H_4OH)Ar_2.$$

The idea behind these experiments was that the benzene nucleus in phenols is more nucleophilic than in acylated aromatic amines. The experiments were performed in presence of anhydrous tin chloride between the anilide or α-naphthalide of benzilic acid and the p-phenetidide of 4,4'-dimethoxybenzilic acid on the one hand with phenol and resorcinol on the other hand (expts. 12, 13 and 14). In this case also, condensation proceeds with formation of monomeric cyclic systems. The data that we obtained indicate that intermolecular reaction will be more probable with those aryl amides whose intramolecular ring closure is hindered by the great distance between their end groups.

EXPERIMENTAL

Di-(1-phenyl-3-butylamide) of oxalic acid and the ethyl ester of 1-phenyl-3-butyl-oxamic acid (expt. 1). To a solution of 16 g 1-phenyl-3-aminobutane* in 20 ml alcohol was added 20 g ethyl oxalate. At the close of the reaction the mass was heated on the water bath until it gave a neutral reaction to litmus. Di-(1-phenyl-3-butylamide) of oxalic acid came down on cooling. It was filtered off and recrystallized from alcohol. Colorless needles, m.p. 170-172°; insoluble in water; soluble on heating in alcohol, benzene and toluene. Yield 0.5 g or 2.6 % of the theoretical, calculated on the 1-phenyl-3-aminobutane taken.

0.0358 g substance: 19.7 ml 0.01 N H_2SO_4. 0.0390 g substance: 21.1 ml 0.01 N H_2SO_4. Found %: N 7.72, 7.61. $C_{22}H_{28}O_2N_2$. Calculated %: N 7.96.

The main product of the reaction was separated from the alcoholic filtrate. After removal of the solvent, the residue was distilled in vacuum to give a colorless, oily liquid with b.p. 183.5-185° (4 mm). Yield 13.5 g or 51% of the theoretical.

d_4^{20} 1.0821; n_D^{20} 1.5135; MR_D 69.21; calculated 68.52.

0.0228 g substance: 8.9 ml 0.01 N H_2SO_4. 0.0208 g substance: 8.1 ml 0.01 N H_2SO_4. Found %: N 5.47, 5.45. $C_{14}H_{19}O_3N$. Calculated %: N 5.62.

Amide of 1-phenyl-3-butyloxamic acid (expt. 2). Gaseous ammonia was passed into a cooled alcoholic solution of 1 g ethyl ester of 1-phenyl-3-butyloxamic acid. The precipitate was filtered and crystallized from alcohol. Slender, colorless needles with m.p. 180°. Yield 0.8 g or 91% of the theoretical.

The amide is insoluble in water, readily soluble in hot alcohol, benzene and toluene.

0.0166 g substance: 11.4 ml 0.01 N H_2SO_4. 0.0146 g substance: 14 ml 0.01 N H_2SO_4. Found %: N 13.32, 13.41. $C_{12}H_{16}O_2N_2$. Calculated %: N 12.72.

1-Phenyl-3-butylamide of benzilic acid (expt. 3). To the phenyl magnesium bromide prepared from 15.7 g (0.1 mole) bromobenzene and 2.3 g (0.1 mole) magnesium in 50 ml ether was added a solution of 5 g (0.02 mole) ethyl ester of 1-phenyl-3-butyloxamic acid. The reaction product was recrystallized from 100 ml 70% alcohol. Colorless needles with m.p. 83°. The compound is sparingly soluble in gasoline, easily soluble in other organic solvents. With concentrated sulfuric acid it gives a brown coloration which changes to green and then to weak-yellow. Yield 4 g or 55.5% of the theoretical.

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* 1-Phenyl-3-aminobutane was prepared by the Leuckhardt reaction from benzylacetone and ammonium formate in 56% yield. B.p. 100° (12 mm). Literature: 101-102° (14 mm) [14].

0.1066 g substance: 4.5 ml 0.01 N H_2SO_4. 0.0304 g substance: 7.6 ml 0.01 N H_2SO_4. Found %: N 3.8, 3.5. $C_{24}H_{25}O_2N$. Calculated %: N 3.9.

Lactam of 2-(γ-aminobutyl)-triphenylacetic acid (expt. 4). Starting substances: a solution of 1 g 1-phenyl-3-butylamide of benzilic acid in 6.5 ml glacial acetic acid and 17 ml conc. sulfuric acid. A brown color was first developed and changed gradually to green. Toward the end of the reaction the solution acquires a yellow-orange color. The reaction mass was poured into 50 ml water and the resultant precipitate was worked up in the usual manner. Crystallization from glacial acetic acid gave a fine crystalline powder with m.p. 153°. Readily soluble in alcohol and acetic acid, more difficultly soluble in benzene and toluene. Yield 0.5 g or 52% of the theoretical.

0.0366 g substance: 10 ml 0.01 N H_2SO_4. 0.0177 g substance: 5.2 ml 0.01 N H_2SO_4. 0.0094 g substance: 0.1028 g camphor: Δt 11.2°. 0.0120 g substance; 0.1240 g camphor: Δt 11.5°. Found %: N 3.82, 4.11; M 326.6, 336.6. $C_{24}H_{23}ON$. Calculated %: N 4.11; M 341.

α-Phenylethylamide of p-tolylic acid (expt. 5). Materials: 6.6 g (0.03 mole) ethyl ester of α-phenylethyloxamic acid, 26.16 g (0.12 mole) p-iodotoluene and 2.76 g (0.12 mole) magnesium. The reaction product slowly crystallizes from benzene in the form of colorless plates with m.p. 112°. Readily soluble in the common organic solvents. With conc. sulfuric acid it forms a transient red color. Yield 1.5 g or 13.7% of the theoretical.

0.0356 g substance: 10.7 ml 0.01 N H_2SO_4. 0.0348 g substance: 9.7 ml 0.01 N H_2SO_4. Found %: N 4.21, 3.9. $C_{24}H_{25}O_2N$. Calculated %: N 3.9.

α-Phenylethylamide of 4,4'-dimethoxybenzilic acid (expt. 6). The reaction was performed between 6.63 g (0.03 mole) ethyl ester of α-phenylethyloxamic acid and p-anisyl magnesium iodide prepared from 28 g (0.12 mole) p-iodoanisole and 2.91 g (0.12 mole) magnesium in 120 ml ether. After decomposition of the reaction mass and distillation of the volatile products with stream, there remained a brown substance with an oily consistency. This was dissolved in alcohol. After standing for 24 hours, the solution deposited colorless long needles with m.p. 96°. Yield 2.6 g or 22% of the theoretical. Insoluble in water and readily soluble in common organic solvents. With conc. sulfuric acid it forms a stable crimson coloration.

0.0230 g substance: 5.8 ml 0.01 N H_2SO_4. 0.0250 g substance: 6.7 ml 0.01 N H_2SO_4. Found %: N 3.53, 3.74. $C_{24}H_{25}O_4N$. Calculated %: N 3.58.

β-Phenylethylamide of 4,4'-dimethoxybenzilic acid (expt. 7). Starting materials: 5 g (0.023 mole) ethyl ester of β-phenylethyloxamic acid, 26.5 g (0.113 mole) p-iodoanisole and 2.7 g (0.113 mole) magnesium. Crystallizes slowly from alcohol in long needles, m.p. 107-108°. Yield 3.8 g or 43% of the theoretical. Insoluble in water and readily soluble in organic solvents. With conc. sulfuric acid it forms a stable crimson coloration.

0.0272 g substance: 7.3 ml 0.01 N H_2SO_4. 0.0494 g substance: 12.4 ml 0.01 N H_2SO_4. Found %: N 3.75, 3.52. $C_{24}H_{25}O_4N$. Calculated %: N 3.58.

Attempt to form a heterocycle from α- and β-phenylethylamides of 4,4'-dimethoxybenzilic acid (expt. 8). Experiments were performed in identical conditions. We describe an experiment with α-phenylethylamide of 4,4'-dimethoxybenzilic acid. To a solution of 0.5 g α-phenylethylamide of 4,4'-dimethoxybenzilic acid in 5 ml glacial acetic acid was added 0.1 ml conc. sulfuric acid. The resultant crimson coloration did not disappear after standing for 120 hours. After this, the reaction mixture was heated for 3 hours on the water bath. The solution, which did not lose its color even after heating, was poured into 20 ml water. Yield 0.4 g air-dry substance, equivalent to 80% of the amount of α-phenylethylamide of 4,4'-dimethoxybenzilic acid taken for the reaction. Needles (from alcohol), m.p. 94-96°. A mixed sample with an authentic specimen of α-phenylethylamide of 4,4'-dimethoxybenzilic acid did not give a depression of melting point.

In an experiment with the β-phenylethylamide of 4,4'-dimethoxybenzilic acid the same results were obtained: about 80% was recovered unchanged. After recrystallization from alcohol the substance had the melting point of the original product (107-108°) and a mixed melting test with the original substance did not give a depression.

Anilide of p-benzoylbenzoic acid (expt. 9). This was prepared by the Bodroux reaction [15]. To the phenyl magnesium bromide prepared from 5.5 g (0.05 mole) ethyl bromide, 1.5 g magnesium and 5.1 g (0.05 mole) aniline in 30 ml ether was added a solution of 5.5 g (0.02 mole) methyl ester of p-benzoylbenzoic acid in 15 ml ether.

After heating for a short period, the reaction mass was decomposed with 5% hydrochloric acid. Needles (from toluene) with m.p. 163-164°. The literature [16] gives 171°.

Anilide of p-triphenylcarbinol carboxylic acid (expt. 10). Starting materials: 1.7 g (0.0056 mole) p-benzoylbenzoic acid anilide, 5.1 g (0.025 mole) iodobenzene and 0.6 g magnesium. Decomposition of the reaction mass with saturated ammonium chloride solution and removal of the ether left a solid mass which crystallized from alcohol. M.p. 182°. Yield 1.7 g or 80% of the theoretical. The literature [17] reports a m.p. of 182° for the anilide of p-triphenylcarbinol carboxylic acid. With 70% sulfuric acid the anilide forms a yellow coloration; with conc. hydrochloric acid it does not give a coloration.

Found %: N 3.66, 3.52. $C_{26}H_{21}O_2N$. Calculated %: N 3.69.

Attempt to cyclize the anilide of p-triphenylcarbinol carboxylic acid (expt. 11). To an acetic acid solution of 0.2 g anilide of p-triphenylcarbinol carboxylic acid was added 2 ml conc. sulfuric acid. A dark-red color appeared and did not disappear on heating the reaction mass on a water bath for 30 minutes. The product was isolated by the usual procedure. Colorless crystals (from alcohol), m.p. 182°. A mixed sample with the original substance melted without depression.

3,3-Bis-(4-methoxyphenyl)-5-ethoxyoxindole (expt. 12). To a solution of 2 g (0.006 mole) p-phenetidide of 4,4'-dimethoxybenzilic acid and 0.8 g (0.009 mole) phenol in 20 ml benzene was added 2 g (0.008 mole) anhydrous tin chloride. The reaction mass was heated for a brief period on a water bath until the red-violet color had disappeared. After cooling, the contents of the flask were poured into 50 ml water. The benzene layer was separated and evaporated to a small volume on a water bath. A crystalline mass separated on standing. Needles (from alcohol) with m.p. 179-180°, in agreement with the data for the previously described 3,3-bis-(4-methoxyphenyl)-5-ethoxyoxindole [18]. A mixed sample gave no depression. Yield 1.5 g or 78%.

3,3-Diphenyl-6,7-benzooxyindole (expt. 13). Reagents: 1.5 g (0.004 mole) α-naphthalide of benzilic acid, 0.5 g (0.004 mole) resorcinol in 20 ml benzene and 2 g (0.008 mole) anhydrous tin chloride. Yield 1.4 g or 98%. Needles (from alcohol) with m.p. 254°, in agreement with the literature data for 3,3-diphenyl-6,7 benzooxyindole [19]. A mixed melting point test did not give depression.

3,3-Diphenyloxyindole (expt. 14). Reagents: 3 g (0.011 mole) benzilic acid anilide, 1.1 g (0.011 mole) phenol and 3.0 g (0.012 mole) tin chloride. Crystallization from benzene gave small rods with m.p. 225°. These data agree with those for 3,3-diphenyloxyindole [20]. A mixed sample with an authentic specimen melted without depression. Yield 2 g or 75.5%.

SUMMARY

1. Intramolecular condensation was effected of the 1-phenyl-3-butylamide of benzoic acid and the possibility was thereby demonstrated of obtaining 8-membered ring systems by intramolecular condensation of aryl amides of hydroxycarboxylic acids.

2. The velocity of closure of the heterocycle in aryl amides of hydroxy carboxylic acids falls in the order: 5>6>7>8, which is consistent with data for carbon rings.

3. In the formation of 5-, 6-, 7- and 8-membered heterocycles in aryl amides of hydroxy carboxylic acids, apart from the distance factor, the reactivity of the same end groups enters into play as a factor in the formation of cyclic systems.

The size limitation on intramolecular condensation of aryl amides of hydroxy carboxylic acids depends on the reactivity of the end groups. Introduction of electron-accepting substituents in the phenyl radicals at the carbonyl carbon makes possible the formation of a larger ring than when electron-donating substituents are introduced.

4. The unsuccessful attempt to close the ring in the anilide of p-triphenylcarbinol carboxylic acid is explained by the great strain in formation of the ring.

5. On the basis of data for closure of heterocycles in aryl amides of hydroxy carboxylic acids, it is shown that for organic compounds capable of ring closure by an ionic mechanism, neither dilution nor vacuum is necessary for isolation of the molecules since the presence of a charge suppresses the reaction of intermolecular interaction.

6. Intermolecular reaction does not take place when arylamides of α-hydroxy carboxylic acids are treated with phenols in presence of anhydrous tin chloride; only products of intramolecular reaction are formed.

7. Anhydrous tin chloride can be successfully utilized for the intramolecular closure of heterocycles in aryl amides of α-hydroxy carboxylic acids.

8. A series of previously undescribed aryl amides of α-hydroxy carboxylic acids and heterocyclic and other compounds were prepared and their properties studied.

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*** See Consultants Bureau English translation, page 761 ff.

**** See Consultants Bureau English translation, page 2063 ff.

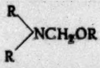
***** See Consultants Bureau English translation, page 359 ff.

****** See Consultants Bureau English translation, page 1877 ff.

REACTION OF ORGANOMAGNESIUM COMPOUNDS WITH DERIVATIVES OF 3,4-DIHYDRO-3-ALKYL-1,3-2-BENZOXAZINES

K. G. Mizuch

The reactivity of compounds containing a methylene group linked to various atoms other than carbon is known to be increased in comparison with similarly structured compounds whose methylene group is linked to identical atoms. As an example we may cite the greater ease of reaction of dialkylaminomethylalkyl ethers (I) with organomagnesium compounds by comparison with compounds of the type of acetals (II) [1]. Examples of compounds whose increased reactivity is caused by the presence of another atomic grouping are α-halomethyl ethers (III) and chloromethylenedialkylamines (IV) [2].



R_2NCH_2OR

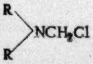
(I)

$ROCH_2OR$

(II)

$ClCH_2OR$

(III)



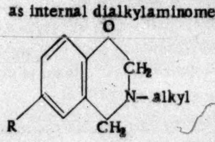
R_2NCH_2Cl

(IV)

As was shown by the author and Ts. M. Gelfer [3], the effect of non-carbon atoms—intensified in some cases by the action of the electrophilic phenyl group—on the methylene group of certain carbonium ethers may be so great as to provoke a more or less complete shifting of the center of electrophilic activity in the ether molecule from the carbonyl carbon to the carbon of the methylene group.

In all the specified types of compounds the atomic groupings [$>NCH_2O-$, $>NCH_2Cl$, $ClCH_2O-$, $BrCH(C_6H_5)O-$], giving rise to an especially easy or uncharacteristic (for these compounds) course of reaction, are partly open chains. It was a matter of interest to investigate the behavior of compounds whose $>NCH_2O-$ grouping was part of a ring.

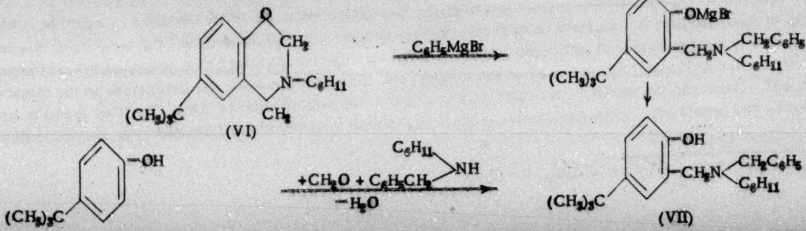
It seemed to us that this problem might be solved by studying the behavior of organomagnesium compounds toward the recently synthesized derivatives of 3,4-dihydro-3-alkyl-1,3,2-benzoxazine (V) [4] which may be regarded as internal dialkylaminomethylphenyl ethers.



(V)

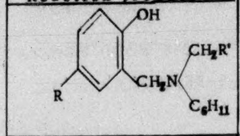
Due to the presence of the $>NCH_2O-$grouping in the ring, compounds (V) differ from dialkylaminomethylalkyl ethers in being more stable. Whereas dialkylaminomethylalkyl ethers are cleaved even in the cold by traces of acids to form the original components (secondary amine, alcohol and formaldehyde), compounds (V) are capable of forming hydrochlorides and only lose formaldehyde when heated with acid [4,5]. It was therefore suggested that the action on (V) of organomagnesium compounds would be accompanied by attack of the nucleophilic radical of the organomagnesium compound on the carbon of the methylene group with consequent ring-opening and formation of 2-dialkylaminomethyl derivatives of phenol, although the reaction itself may be expected to be less intensive than in the case of ethers (I).

For the purpose of putting this theory to the test, we reacted phenyl magnesium bromide with 3,4-dihydro-3-cyclohexyl-6-tert. butyl-1,3,2-benzoxazine (VI), and we established that the reaction is energetic and is accompanied by appreciable rise of temperature. After decomposition of the reaction mixture with ammonium chloride, the main reaction product was a substance melting (from ethyl alcohol) at 137-137.5° and differing from the original benzoxazine. The elementary analysis gave the formula $C_{24}H_{33}ON$. The compound contained one active hydrogen atom. This enabled the structure 2-(benzylcyclohexylaminomethyl)-4-tert. butylphenol (VII) to be assigned to it. The structure of (VII) was confirmed by its identification with the substance prepared by known method by direct reaction of N-cyclohexylbenzylamine with formaldehyde and 4-tert. butylphenol.



(VI)

(VII)

R"MgX	Reaction product 		Method of isolation	Yield (%)	Melting point	Formula
	R	R'				
CH_3MgI	$(CH_3)_3C$	CH_3	A	82.2	85.4-86*	$C_{19}H_{31}ON$
$(CH_3)_2CHCH_2MgBr$	$(CH_3)_3C$	$(CH_3)_2CHCH_2$	A	79	63.2-64*	$C_{22}H_{37}ON$
$CH_2{=}CHCH_2MgBr$	$(CH_3)_3C$	$CH_2{=}CHCH_2$	A	85.5	46.8-47.5*	$C_{21}H_{33}ON$
$C_6H_{11}MgCl$	$(CH_3)_3C$	C_6H_{11}	A	87	101.2-101.8**	$C_{24}H_{39}ON$
C_6H_5MgBr	$(CH_3)_3C$	C_6H_5	B	82.5	137 -137.5*	$C_{24}H_{33}ON$
C_6H_5MgBr	C_6H_5	C_6H_5	B	92.8	117.2-117.8***	$C_{26}H_{29}ON$
$C_6H_5CH_2MgCl$	$(CH_3)_3C$	$C_6H_5CH_2$	B	93	136.6-137.2****	$C_{25}H_{35}ON$

Note. Purification: * from ethyl alcohol; ** from methyl alcohol; *** from methyl alcohol-ethyl acetate (2:1);

Attention should be drawn to the fact that Burke and co-workers [5] had treated compounds of type (V) with CH_3MgI for determination of their active hydrogen, but had not observed a reaction with organomagnesium compounds. In a more recent publication [6], which appeared after the completion of the experimental part of the present investigation, Burke and co-workers reported the preparation of 1-dibenzylaminomethyl-2-naphthol in 8% of the theoretical yield by the action of a large excess of C_6H_5MgBr on 2,3-dihydro-2-benzyl-1H-naphth [1,2-e]-m-oxazine. Since our own data gave a clearer idea of the course of the reaction of 3,4-dihydro-3-alkyl-1,3,2-benzoxazines with organomagnesium compounds than could be derived from paper [6], we decided to publish our results.

Our work differed from [6] in that the transformation in question was realized not only with C_6H_5MgBr but also with a series of other organomagnesium compounds. When (VI) was reacted with methyl magnesium iodide, isobutyl magnesium bromide, allyl magnesium bromide, benzyl magnesium chloride and phenyl magnesium bromide, the yields of the isolated pure dialkylaminomethyl derivatives were 79-93% of the theoretical. A benzoxazine with another structure was tested in the shape of 3,4-dihydro-3-cyclohexyl-6-phenyl-1,3,2-benzoxazine *, from which was prepared — by treatment with phenyl magnesium bromide — 2-(benzylcyclohexylaminomethyl)-4-phenylphenol in over 90% yield. These data show beyond doubt that ring-opening with formation of 2-dialkylaminomethyl derivatives of phenol is the main direction of the reaction.

The effect of the sterically hindered organomagnesium compounds was investigated by carrying out the reaction of (VI) with tert. butyl magnesium bromide and cyclohexylmagnesium chloride. Also in this case the reaction proceeded according to the same scheme and the products were 2-(2,2-dimethylpropylcyclohexylaminomethyl)-4-tert. butylphenol and 2-(cyclohexylhexahydrobenzylaminomethyl)-4-tert. butylphenol.

Special interest is attached to the preparation of 2-dialkylaminomethyl derivatives of phenols by the action of organomagnesium compounds on derivatives of 3,4-dihydro-3-alkyl-1,3,2-benzoxazine in connection with recent studies of this type of compound as therapeutic agents [7]. By the classical method of preparation of 2-dialkylaminomethyl derivatives of phenols containing various substituents at the nitrogen, it is necessary to start from formaldehyde and the appropriate secondary amines whose synthesis involves well-known difficulties and gives low yields [8]. The reaction utilizing derivatives of 3,4-dihydro-3-alkyl-1,3,2-benzoxazines and organomagnesium compounds enables the preparation of 2-dialkylaminomethyl derivatives of phenols with high yields and wide diversification of the substituents in the resultant N-dialkylaminomethyl group.

EXPERIMENTAL

Reaction of (V) with organomagnesium compounds was performed in an ethereal medium by addition, with stirring, of the crystalline benzoxazine to an excess of organomagnesium compound freed from residues of magnesium. The amount of organomagnesium compound varied in individual experiments from 2 to 4 moles per mole of benzoxazine. During the addition of the benzoxazine the temperature of the reaction mass was maintained in the range of −5° to +5°. Thereupon the mixture was heated a short period at the boiling point of ether. Reaction products were isolated by two procedures. When the reaction product was soluble in ether, it was extracted after decomposition of

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* Formula (V) where alkyl = cyclo-C_6H_{11}, R = C_6H_5.

Calculated (%)			Found (%)		
C	H	N	C	H	N
78.84	10.80	4.84	78.71	10.73	4.84
79.70	11.25	4.22	79.78	11.25	4.40
79.95	10.54	4.44	79.84	10.68	4.65
80.61	11.00	3.92	80.58	11.17	4.04
82.00	9.46	3.99	81.95	9.34	4.25
84.05	7.87	3.77	84.25	7.99	3.70
82.14	9.65	3.83	82.34	9.68	3.88

**** from ethyl acetate.

the reaction mixture with ammonium chloride solution. The ethereal extract was dried with sodium sulfate and the substance was isolated after evaporation of the ether (variant A). When the substance was poorly soluble in ether, the latter was evaporated from the reaction mixture after its decomposition with ammonium chloride solution and the product (insoluble in the obtained aqueous solution) was filtered off and dried at room temperature (variant B). The substance was purified by crystallization from organic solvents. In the table are set forth the results of the action of some $R''MgX$ on benzoxazines.

2-(Benzylcyclohexylaminomethyl)-4-tert. butylphenol (VII) from N-benzylcyclohexylamine hydrochloride, formaldehyde and 4-tert.butylphenol. The starting N-benzylcyclohexylamine hydrochloride was prepared in the conditions described in [8] by reduction of N-cyclohexylidenebenzylamine with 99% HCOOH followed by treatment with hydrochloric acid. The hydrochloride was purified by crystallization from a mixture of isopropyl alcohol and ether and melted at 284-285° (block); the literature gives 252-253° [9], 284° [10].

For the preparation of (VII), successive addition of 2.25 g N-benzylcyclohexylamine hydrochloride, 0.4 g paraformaldehyde and 1.5 g 4-tert. butylphenol was made to a solution of 0.6 g KOH in 15 ml ethyl alcohol. The mixture was heated on a water bath, cooled, and diluted with water. The separated product was crystallized from ethyl alcohol and then melted at 136.2-136.8°. A mixed test with the product of interaction of C_6H_5MgBr with (VI) did not give a melting point depression.

SUMMARY

1. Reaction of organomagnesium compounds with 3,4-dihydro-3-alkyl-6-alkyl(aryl)-1,3,2-benzoxazines results in opening of the benzoxazine ring with formation of the corresponding 2-(dialkylaminomethyl)-4-alkyl(aryl)-phenols as the main products.

2. The method in question may possess preparative interest, since it enables the introduction of a wider variety of substituents in the formed N-dialkylaminomethyl group.

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APPLICATION OF THE WILLGERODT REACTION TO THE SYNTHESIS OF SUBSTITUTED PHENYL- AND NAPHTHYLACETIC ACIDS

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Application of the Willgerodt reaction to the synthesis of a fairly large number of phenylacetic acids has been described in the literature [1]; in the majority of cases, however, the yields are not stated and it is therefore impossible to assess the value of this method for synthesis of a particular compound. More detailed data have been published on the preparation of thiomorpholides from substituted acetophenones [2,3,4,5], but due to the difficulty of saponification of the former, this modification of the Willgerodt reaction is little suited to the synthesis of the corresponding phenylacetic acids [6]. This reaction has not been applied, however, to the synthesis of substituted naphthylacetic acids. Moreover, the Willgerodt reaction is undoubtedly interesting for the synthesis in laboratory conditions of a whole series of substituted phenylacetic acids whose preparation is more complicated by other methods.

Nearly all of the phenyl- and naphthylacetic acids were prepared by us in standardized conditions: heating of ammonium polysulfide and the appropriate ketone in aqueous dioxane solution. Our experimental data on the preparation of phenyl- and naphthylacetic acids are set forth in Table 1.

It should be noted that it was not possible to obtain the corresponding amides and acids from o-hydroxyacetophenone, p-hydroxyacetophenone, 2,5-dibromoacetophenone, 2,4-dimethoxyacetophenone, 2,4,5-trichloroacetophenone, 4-bromonaphthyl-1-methyl ketone, 4-chloronaphthyl-1-methyl ketone, 4-methoxynaphthyl-1-methyl ketone and 4-ethoxynaphthyl-1-methyl ketone. The data of Table 1 permit of several generalizations about the effect of substituents in the aromatic radical on the course of the Willgerodt reaction. In spite of the abundant experimental material, this question has received very little attention in the literature. It has merely been reported that the presence of alkyl and alkoxyl and halogens has no appreciable influence on the course of the reaction [1], whereas nitro-, amino-, formyl and similar groups may undergo changes due to the occurrence in the reaction medium of oxidation-reduction processes.

Our experimental data give definite indication of the influence of even such substituents as halogen and alkyl on the course of the Willgerodt reaction. The presence of one substituent in the phenyl radical in the para-position to the acetyl lowers the yield of the normal reaction products. The simplest substituents may be arranged in the following order of increasing unfavorable influence on the yield of products of the Willgerodt reaction:

$$CH_3 < Cl < CH_3O < I < OH.$$

The main reaction product in the presence of such substituents as Cl, I, and OCH_3 is a mixture of 2,4- and 2,5-substituted thiophenes.

Introduction of a second substituent into the aromatic radical suppresses the reaction of formation of thiophenes, in consequence of which the yield of phenylacetic acids and their amides sharply increases. Thus, 4-methoxy-2-methyl- and 4-methoxy-3-methylacetophenones give considerably higher yields of normal products of reaction than 4-methoxyacetophenone, while nearly quantitative yields of amides and acids are got from some haloalkylacetophenones.

Accumulation of more than two halogens or other substituents in the aromatic radical of acetophenone leads to lowering of the yield of normal products of the Willgerodt reaction. In such a case the effect of halogens is particularly marked; the influence of methyl groups is considerably weaker.

A similar picture is observed in the naphthalene series. 4-Methylnaphthyl-1-methyl ketone is converted in satisfactory yield into 4-methylnaphthylacetamide, whereas the corresponding chloro-, bromo- and alkoxy ketones give mainly products of resinification. With ethyl-, propyl and butylnaphthylmethyl ketones the reaction proceeds normally but the yield of amides falls with increasing molecular weight of the hydrocarbon radical.

EXPERIMENTAL

Preparation of all of the amides of phenylacetic acids was performed in the following standard conditions: in a glass tube, volume about 100 ml, were placed 5 g ketone, 20 ml dioxane and 25 ml aqueous solution of ammonium polysulfide. The tube was placed in a stainless steel rotating autoclave and kept at 165-170° for 4 hours. After cooling, the reaction mixture was transferred to a porcelain beaker and evaporated on the water bath to dryness. The residue was twice extracted with hot water (each time with 300 ml). The precipitate of amide which came down on cooling the aqueous extract was filtered off and recrystallized. The filtrate was evaporated to a small volume and a small additional amount of amide was thus obtained; in some cases, acidification of the mother liquor gave a small amount of acid which was filtered and recrystallized from water. In Table 2 are set forth the data for compounds not described in the literature.

TABLE 1

Prep. No.	Name of starting ketone	Yield (%)		M.p. of amide	M.p. of acid
		of amide	of acid		
1	Acetophenone	88	5.5	–	–
2	4-Chloroacetophenone	28	7	175*[175]	105* [105.5]
3	4-Iodoacetophenone	12	0	*	135 [135]
4	4-Methylacetophenone	63	0	184 [185]	92 [92]
5	2-Hydroxyacetophenone	0	0	–	–
6	4-Hydroxyacetophenone	0	0	–	–
7	4-Methoxyacetophenone	25	0	175 [175]	85 [85]
8	2,5-Dibromoacetophenone	0	0	–	–
9	2,4-Dichloroacetophenone	39	5.5	*	*
10	2,5-Dichloroacetophenone	34.7	0	175 [175]	106 [106]
11	3-Methyl-4-bromoacetophenone	68	0	165 [168]	81 [81]
12	3-Methyl-6-bromoacetophenone	74.7	4	152 [152]	82 [82]
13	3-Methyl-4-chloroacetophenone	72.4	0	162 [162]	83 [83]
14	3-Methyl-6-chloroacetophenone.	87.8	5.2	141 [141]	86 [85]
15	4-Methyl-2-chloroacetophenone.	74.8	0	*	*
16	2-Methyl-4-methoxyacetophenone	59.2	0	*	107 [107]
17	3-Methyl-4-methoxyacetophenone.	61.8	0	*	127 [127]
18	2,4-Dimethoxyacetophenone	0	0	–	–
19	2,4,5-Trichloroacetophenone	0	0	–	–
20	2,4,5-Trimethylacetophenone	42.1	0	165 [165]	118 [118]
21	Methyl-1-naphthyl ketone	87.8	0	182	132
22	4-Bromonaphthyl-1-methyl ketone	0	0	–	–
23	4-Chloronaphthyl-1-methyl ketone.	0	0	–	–
24	4-Methylnaphthyl-1-methyl ketone.	86.3	0	209 [209]	148 [148]
25	4-Methoxynaphthyl-1-methyl ketone	20	0	*	*
26	4-Ethylnaphthyl-1-methyl ketone	41	0	*	*
27	4-Ethoxynaphthyl-1-methyl ketone.	0	0	–	–
28	4-Propylnaphthyl-1-methyl ketone.	40	0	*	*
29	4-Butylnaphthyl-1-methyl ketone.	34	0	*	*

Note. The melting points of amides and acids in brackets are literature data.

SUMMARY

1. Starting from the corresponding ketones, a study was made of the preparation of substituted phenyl- and naphthylacetic acids by the Willgerodt reaction. A large number of compounds were used in the investigation.

2. It was established that the yield of arylacetic acids prepared by the Willgerodt reaction largely depends on the character of the substituents in the aromatic radical. In the simplest case, substituents unfavorably influencing the yield of arylacetic acids are arranged in the following order:

$$CH_3 < Cl < CH_3O < I < OH.$$

Introduction of a second substituent into the aromatic radical leads to fall in the yield of normal products of the Willgerodt reaction.

3. A number of the synthesized compounds have not been described in the literature.

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* See Table 2.

TABLE 2

Prep.	Name of compound	Melting point		Analysis					
		acid	amide	Wt. of sample (g)	Amount of 0.02 N KOH or H_2SO_4 (ml) consumed	Molecular weight		N content (%)	
						found	calculated	found	calculated
1	4-Iodophenylacetamide	–	191*	0.0624	11.81	–	–	5.30	5.36
2	2,4-Dichlorophenylacetic acid	131*	168-169	0.0652	16.15	201.9	204.8	–	–
				0.0532	13.24	201.0		–	–
3	2-Chloro-4-methylphenylacetic acid	106	164	0.0840	22.54	186.3	184.4	–	–
				0.0795	21.44	185.4		–	–
4	4-Methoxy-2-methylphenylacetamide	–	154	0.0742	20.19	–	–	7.62	7.80
				0.0720	19.64	–	–	7.64	
5	4-Methoxy-3-methylphenylacetamide	–	153	0.0690	19.00	–	–	7.71	7.80
				0.0698	18.67	–	–	7.49	
6	4-Methoxynaphthyl-1-acetic acid	144	175	0.1432	13.11*	218.5	216	–	–
				0.1238	11.28*	219.4		–	–
7	4-Ethylnaphthyl-1-acetic acid	129	167	0.0852	19.36	220.0	214	–	–
				0.0831	18.92	219.6		–	–
8	4-Propylnaphthyl-1-acetic acid	119	157	0.0892	19.30	231.0	228	–	–
				0.0901	19.35	232.8	–	–	–
9	4-Butylnaphthyl-1-acetic acid	110	156	0.0841	17.23	244.0	242	–	–
				0.0731	15.01	243.5		–	–

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SOME 9-SUBSTITUTED DERIVATIVES OF ACRIDINE

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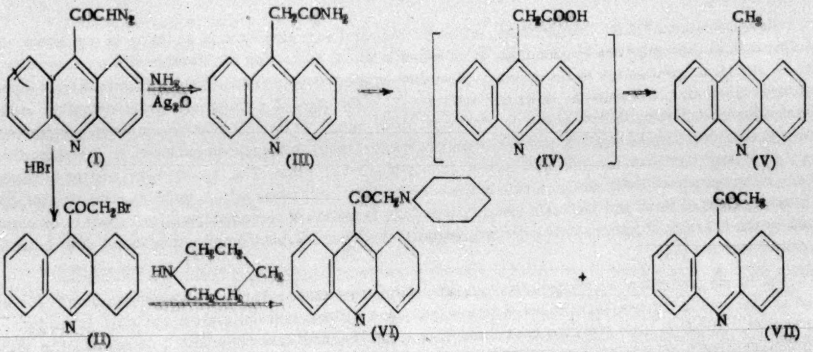
One of us in collaboration with T. V. Gortinskaya [1] has described 9-(diazoacetyl)-acridine (I), as well as acridyl-9-(ω-bromomethyl ketone) (II) which was prepared from diazoacetylacridine by the action of hydrogen bromide. Starting from these compounds, we undertook the synthesis of some previously unknown 9-substituted derivatives of acridine: from diazoacetylacridine we wished to obtained (by Wolff's method) acridyl-9-acetic acid (IV), while by condensation of acridyl bromomethyl ketone with secondary amines we aimed at obtaining the corresponding amino ketones.



Attempts to prepare acridylacetic acid directly from diazoacetylacridine were not crowned with success. It was therefore resolved first to prepare acridyl-9-acetamide (III) and then to saponify it to the acid. Transformation of diazoacetylacridine into acridylacetamide proceeds very smoothly and gives a yield of about 80% of the theoretical. On treating acridylacetamide with sodium nitrite in solution in a mixture of sulfuric and acetic acids, we actually succeeded in obtaining an acid whose analysis agreed fairly closely, but not entirely satisfactorily, with that calculated for acridylacetic acid. With the aim of identifying this acid, it was converted into the hydrochloride of the acid chloride by the action of thionyl chloride in benzene solution; the acid chloride was then treated with concentrated aqueous ammonia to form the amide. The decomposition temperature of the latter proved to be 3° lower than that of the acridylacetamide prepared from diazoacetylacridine. A mixed sample of the two amides, however, gave a 20° depression of decomp. point. Attention was then directed to the fact that the conjectured acridylacetic acid, the hydrochloride of the acid chloride and the amide had decomposition temperatures respectively agreeing with those of acridine-9-carboxylic acid, the hydrochloride of its chloride, and the amide. It was further established that a mixture of the conjectured acridylacetic acid with authentic acridine-carboxylic acid, likewise a mixed sample of the amides of both acids, do not give a depression of the decomposition temperature, and that, consequently, the action of nitrous acid on acridylacetamide leads to acridine-carboxylic acid. The reason for this unexpected result became clear when acridylacetamide was subjected to hydrolysis in an alkaline or acid medium. Boiling of acridylacetamide with 20% hydrochloric acid gives a good yield of a substance which is insoluble in alkali and whose analysis, melting point and other properties indicate it to be 9-methylacridine (V). 9-Methylacridine is also formed by hydrolysis of acridylacetamide with alcoholic alkali, but side by side with acridone. Formation of 9-methylacridine in this case conclusively shows that hydrolysis of acridylacetamide does indeed give acridine-9-acetic acid, which is apparently unstable and undergoes decarboxylation to 9-methylacridine in the experimental conditions. If the reaction is performed with the help of a large excess of nitrous acid, however, then the intermediately formed 9-methylacridine in the instant of its formation is oxidized to acridine carboxylic acid. In practice, brief heating of acridineacetamide with a small excess of nitrous acid gives 9-methylacridine.

Acridyl-9-(acetoxymethyl ketone) is obtained by reacting diazoacetylacridine with glacial acetic acid in presence of a small amount of copper acetate as catalyst. It is curious that this reaction does not take place in the absence of a catalyst.

The reaction of acridylbromomethyl ketone with piperidine proceeds in an unusual manner. On mixing a solution of acridylbromomethyl ketone in absolute benzene with an excess of piperidine at room temperature, piperidine hydrobromide soon starts to come down from the reaction solution, contaminated with a trace of acridone. After 6 hours the amount of piperidine hydrobromide is about 90% of the theoretical. On this basis we should expect that the condensation of the bromo ketone with piperidine is very complete. Actually, however, this is not the case. After separating the piperidine hydrobromide and driving off the benzene from the filtrate in vacuum, a syrup remains; trituration of the latter with methanol causes a compound with a decomposition temperature of about 130° to separate (precipitate A). It decomposes when recrystallization from methanol or absolute benzene is attempted and partly forms acridone. The same result is obtained when precipitate A is reprecipitated from chloroform by absolute ether at room temperature. Since the various attempts to purify precipitate A were unsuccessful, it was subjected to elementary analysis without purification. The results are close to those calculated for acridyl-9-(piperidinomethyl ketone) (VI). Moreover, it was possible to isolate (as chloroplatinate or picrate) another compound which unexpectedly proved to acridyl-9-(methyl ketone) (VII). After isolation in the free state from the picrate, this compound was identified by comparison with the acridylmethyl ketone prepared by oxidation of 9-α-(hydroxyethyl)-acridine with chromic acid mixture [2].

Debromination of acridylbromomethyl ketone by treatment with piperidine is, as far as we are aware, the first published case of debromination by an amine, of an α-bromo ketone containing the bromine at a primary carbon atom. A similar debromination by the action of piperidine on α-bromoketo esters containing bromine at a secondary or tertiary carbon atom was noted by Howk and McElvain [3] in the cases of α-bromo-α-benzoylacetoethyl, α-bromo-α-benzoylpropioethyl and α-bromo-α-benzoylphenylacetoethyl esters. In the first example, α,α-dipiperidinobenzoyl acetoethyl ester was formed together with the benzoylacetoethyl ester; in the second example, α, β-dipiperidinobenzoylpropioethyl ester was formed in addition to benzoylpropioethyl ester. The intermediate product in these reactions, in the opinion of Howk and McElvain is N-bromopiperidine; this would satisfactorily account for their results. The considerations of Howk and McElvain about intermediate formation of N-bromopiperidine appear to be corroborated by the isolation of nitromalonic ester and N-bromodimethylamine when bromonitromalonic ester is reacted with dimethylamine [4].

During the reaction of acridylbromomethyl ketone with piperidine, evidently N-bromopiperidine is likewise formed in part, and in the conditions of our experiment it reacts with excess of piperidine and gives piperidine hydrobromide. Although little study has been made of the properties of N-bromopiperidine, we nevertheless know that it behaves like N-chloropiperidine; the latter is known to decompose on standing with release of the hydrogen halide of piperidine, while with alcoholic KOH it gives KCl and tripiperideine [5]. Consequently, we can understand why the yield of piperidine hydrobromide in our case reaches 90% of the theoretical, whereas the yield of the amino ketone (precipitate A) is only about 25% on the average.

In order to verify whether piperidine exercises a specific action on acridylbromomethyl ketone, a similar experiment was run with diethylamine in place of piperidine. In this case, also, we obtained acridylmethyl ketone, diethylamine hydrobromide (90% of the theoretical) and a considerable amount of acridone. Acridine-9-(diethylaminomethyl ketone) could not be isolated. This is probably because the reaction solution was allowed to stand for too long a period, in consequence of which the formed amino ketone was able to decompose and form acridone.

Debromination of α-bromo ketones by piperidine in the above indicated cases should undoubtedly be correlated with the known ability of α-bromo ketones to undergo debromination according to the reversible reaction:

$$RCOCHBrR' + HBr \rightleftharpoons RCOCH_2R' + Br_2,$$

in which the equilibrium is more or less shifted to the right or to the left, depending on the structure of the bromo ketone. In the presence of a bromine acceptor (phenol, β-naphthol or cyclohexene), debromination is very complete [6]. Thus, even ω-bromoacetophenone, which is unaffected by hot concentrated hydrobromic acid, is almost completely transformed into acetophenone in a medium of a 33% HBr solution in glacial acetic acid in presence of β-naphthol; the equivalent amount of α-bromo-β-naphthol is formed [6a].

On the basis of the foregoing remarks, the idea suggests itself that debromination of α-bromo ketones by amines cannot be such a rare phenomenon as appears to be the case from the small number of examples reported up to now.

All of the decomposition temperatures reported in this paper were determined as a rule by first heating the capillary rapidly and then, from 40-50°, maintaining a temperature rise of 4° per minute.

EXPERIMENTAL

Acridyl-9-acetamide

Into a three-necked, 100 ml flask fitted with stirrer, mercury seal and reflux condenser are charged 65 ml alcohol, 18 ml conc. aqueous ammonia and 3 ml 10% silver nitrate solution. The mixture is heated to 70-75°, and at this temperature, with stirring, is added (in small portions over a period of 2 hours) 3 g finely pulverized 9-(diazoacetyl)-acridine, the course of the reaction being checked by the evolution of nitrogen. After the reaction solution has completely cooled, the lustrous, dark-brown, fine needles are filtered off and washed with dilute ammonia solution and then with water. Yield of acridylacetamide 2.3 g or 80% of the theoretical. Decomposition point 258-260°.

For analysis, the acridylacetamide was recrystallized from a small quantity of alcohol. White (with a greenish tinge), coalescent needles with decomposition point 260-261°. Acridylacetamide is soluble in glacial acetic acid and in mineral acids; it is reprecipitated unchanged by adding alkali to its solutions in acids prepared in the cold or with gentle heating; purification may be effected by this procedure.

2.895 mg substance: 8.070 mg CO_2; 1.275 mg H_2O. 2.360 mg substance: 0.250 ml N_2 (24°, 743 mm).
Found %: C 76.02; H 4.93; N 11.90. $C_{15}H_{12}ON_2$. Calculated %: C 76.24; H 5.12; N 11.86.

9-Methylacridine from Acridyl-9-acetamide

a) By the action of hydrochloric acid. 1 g acridylacetamide is dissolved in 30 ml 20% hydrochloric acid and refluxed for 1½ hours. The yellow solution is filtered and 12% aqueous ammonia is added until alkaline. The precipitate weighs 0.8 g. M.p. 115-117°. Recrystallization from aqueous alcohol gives lustrous light-yellow needles which lose their luster when dried in the vacuum-desiccator; m.p. 118-119°. A mixed test with a sample of 9-methylacridine does not give a depression.

Found %: C 86.89; H 5.52; N 7.51. $C_{14}H_{11}N$. Calculated %: C 87.01; H 5.74; N 7.25.

b) By the action of alcoholic alkali. 1 g acridylacetamide is boiled for 10 hours with 25 ml 25% solution of KOH in methyl alcohol. At the end of the heating, the whole of the amide goes into solution with a dark, yellowish-green color. The solution is evaporated to dryness in vacuum and the residue is heated with water, drained at the pump and well washed. The dried residue is dissolved in boiling ethyl alcohol; green needles of acridone separate from the filtrate; its m.p. and its mixed m.p. are both 353-354°. After separation of the acridone, the alcoholic mother liquor is diluted with water and yields 0.22 g 9-methylacridine with m.p. 116-117°.

c) By action of nitrous acid. 1 g acridylacetamide is dissolved in 12 ml 96% acetic acid and the solution filtered if necessary; addition is made of 1.8 ml 91% sulfuric acid and the mass is heated to 70°. At this temperature, and with stirring, dropwise addition is made of 2 ml 20% sodium nitrite solution; heating is continued for a further 5 minutes and the mass is poured into 50 ml water. The homogeneous solution is made slightly alkaline with dilute KOH solution. The light-yellow precipitate of 9-methylacridine melts at 115-116° after recrystallization from aqueous alcohol.

Acridyl-9-carboxylic Acid from Acridyl-9-acetamide

0.85 g acridylacetamide is dissolved in 12 ml 96% acetic acid; 1.8 ml 91% sulfuric acid is added, following gradually at room temperature and with stirring by 2.4 g finely pulverized sodium nitrite. The temperature of the solution is then slowly raised to 75-80° and held there for 2 hours. After cooling, the reaction mixture is run into 100 ml cold water; the amorphous yellow precipitate of the acid is drained at the pump and twice purified through its sodium salt. For this purpose the acid is dissolved in 10% soda, filtered, and acidified with dilute hydrochloric acid until the reaction is acid to Congo. The obtained acid weighs 0.45 g and has decomposition point 279-281°. After recrystallization from glacial acetic acid the decomposition point is 283-284°. This is also the decomposition point of its mixture with an authentic specimen of acridine-9-carboxylic acid.

Found %: C 74.68; H 4.39. $C_{14}H_9O_2N$. Calculated %: C 75.31; H 4.07.

0.2 g acid, prepared by the above-described method and purified through the sodium salt, is boiled with a mixture of 1 ml thionyl chloride and 1.2 ml absolute benzene until a homogeneous solution is formed. The excess of thionyl chloride and benzene are distilled off, fresh benzene is added to the residue and again distilled off; this operation is repeated 2-3 times. The dry residue is well washed with benzene and dried. Yield of the hydrochloride of acridine-9-carboxylic acid chloride 0.16 g. Decomposition point 214-215°.

0.15 g of the carboxylic acid chloride hydrochloride is mixed with 10 ml conc. aqueous ammonia, gently heated on the water bath and left overnight. The precipitate, which is no longer crystalline, is drained, washed with water and recrystallized from alcohol. Decomposition point 263-264°. A mixed test with the amide of acridine-9-carboxylic acid prepared by hydrolysis of 9-cyanoacridine [7] does not give a depression. A mixed sample with acridyl-9-acetamide melts at 240-242° with decomposition.

Acridyl-9-(acetoxymethyl Ketone)

6 ml glacial acetic acid, to which has been added a few crystals of copper acetate, is heated to the boil under a reflux condenser, and to the boiling solution is added 1 g 9-(diazoacetyl)-acridine dropwise over a period of 30 minutes. Vigorous evolution of nitrogen soon commences and about 75 ml is collected. After completion of the addition of the diazoacetylacridine, the dark-brown solution is boiled for another few minutes. The cooled solution is heavily diluted with ether and the crystalline precipitate of acridyl-9-(acetoxymethyl ketone) is filtered at the pump. Weight 0.45 g, m.p. 178-179°. A further 0.2 g can be isolated from the mother liquor after evaporation. Same m.p.

After recrystallization from alcohol the pure substance melts at 183-184°. Acridyl-9-(acetoxymethyl ketone) is slightly soluble in benzene and chloroform, almost insoluble in ether and ligroine, soluble in inorganic acids.

3.655 mg substance: 9.808 mg CO_2; 1.554 mg H_2O. Found %: C 73.18; H 4.76. $C_{17}H_{13}O_3N$. Calculated %: C 73.09; H 4.69.

Reaction of Acridyl-9-(ω-bromomethyl ketone) with Piperidine

3 g acridyl-bromomethyl ketone with m.p. 148-150° is dissolved with heating in 53 ml benzene (previously dried over sodium); to the cooled solution is added 3.9 ml dry piperidine and the mass is left in a dark place at room temperature for 6 hours. The crystalline precipitate is filtered, washed with dry benzene and dried. Weight 1.6 g. Treatment with cold water brings the greater part of the material into solution; after driving off the water from the filtrate and recrystallizing from chloroform, the product melts at 234-235°, which is the m.p. of piperidine hydrobromide. The water-insoluble portion, weight about 0.1 g, melts (after purification by sublimation) at 353° and does not give a depression in admixture with acridone.

Evaporation of the benzene filtrate of the reaction solution in vacuum at a temperature not exceeding 30-35° leaves a dark syrup smelling of mice. Trituration of the residue with 20 ml methanol causes separation of 0.65-0.85 g greenish-yellow precipitate (A); this is filtered at the pump and washed several times with methanol. This precipitate melts at 127-130° with decomposition to a dark liquid which rises in the capillary at about 136°. Sparingly soluble in ether, ligroine, benzene and methyl and ethyl alcohols, soluble in the cold in chloroform and glacial acetic acid. An attempt to purify it by recrystallization from benzene or methyl alcohol led to separation from the solution of a small quantity of acridone; removal of the solvent from the filtrate in vacuum at 30-35° gave a dark-brown, oily residue. In most cases a similar result is obtained by reprecipitation with dry ether of the cold-prepared solution of precipitate A in a small quantity of dry chloroform. The elementary analysis of the unpurified precipitate A gives results in fairly close agreement with those calculated for acridyl-9-(piperidinomethyl)-ketone.

2.772 mg substance: 8.151 mg CO_2; 1.612 mg H_2O. 3.212 mg substance 9.415 mg CO_2; 1.830 mg H_2O. 2.985 mg substance: 0.234 ml N_2 (21°, 739.6 mm). 4.085 mg substance: 0.324 ml N_2 (22°, 732.8 mm). Found %: C 80.19, 79.94; H 6.51, 6.38; N 8.87, 8.86; $C_{20}H_{20}ON_2$. Calculated %: C 78.90; H 6.62; N 9.21.

The combined transparent methanol solutions obtained after separation and washing of precipitate A, with a total volume of 35-40 ml, are acidified with 4 ml 10% alcoholic solution of HCl and precipitated with 40 g of 10% alcoholic solution of platinum chloride. After addition of one third of the platinum chloride, the solution is decanted from the resinous precipitate; this operation is repeated once, and then the remaining platinum chloride is added; after a few hours the chloroplatinate is filtered off and twice recrystallized from 3% hydrochloric acid; decomposition point 244-245° with preliminary darkening.

4.005 mg substance: 6.005 mg CO_2; 1.115 mg H_2O. 4.035 mg substance; 0.157 ml N_2 (22°, 751 mm). 4.615 mg substance: 4.322 mg AgCl. 10.915 mg substance: 2.400 mg residue after ignition. 0.1200 g substance: loss in weight 0.048 mg (100°, P_2O_5). Found %: C 40.88; H 3.12; N 4.45; Cl 23.16; Pt 21.99, volatiles 4.05.

The analytical data, with the exception of the nitrogen content, are in agreement with those calculated for the chloroplatinate of acridyl-9-(methyl ketone) crystallizing with two molecules of water. $C_{30}H_{28}O_4N_2Cl_6Pt$. Calculated %: C 40.53; H 3.18; N 3.15; Cl 23.95; Pt 21.98; volatiles 4.05.

The following results for the elementary analysis were obtained after drying in a tube-type desiccator over P_2O_5 at 100°.

3.628 mg substance: 5.616 mg CO_2; 0.995 mg H_2O. 4.090 mg substance: 4.192 mg AgCl. 14.130 mg substance: 3.205 mg residue after ignition. Found %: C 42.17; H 3.07; Cl 25.35; Pt 22.67. $C_{30}H_{24}O_2N_2Cl_6Pt$. Calculated %: C 42.24; H 2.84; Cl 24.97; Pt 22.91.

On adding an alcoholic solution of picric acid to the methanol solution prepared after separation of precipitate A and acidified with 2.1 ml alcoholic HBr solution, the picrate of acridyl-9-(methylketone) comes down; this recrystallizes from methanol in the form of dark-brown (nearly black) needles with decomposition point 245-246°.

2.604 mg substance: 5.347 mg CO_2; 0.768 mg H_2O. 3.335 mg substance: 0.372 ml N_2 (28°, 732.5 mm). Found %: C 56.0; H 3.30; N 12.19. $C_{21}H_{14}O_8N_4$. Calculated %: C 55.99; H 3.13; N 12.45.

The free base obtained from the picrate with the help of hydrochloric acid has m.p. 101-103° (light-yellow needles) after recrystallization from ligroine (b.p. 50-75°).

Found %: C 81.78; H 4.90; N 6.74. $C_{15}H_{11}ON$. Calculated %: C 81.42; H 5.0; N 6.34.

Acridyl-9-(methyl ketone), prepared by Eisleb's method [2] by oxidation of 9-(α-hydroxyethyl)-acridine with chromic acid mixture, also melts at 101-103° and not at 109° (as reported by Eisleb) and does not give a depression in the mixed melting determination.

Reaction of Acridyl-(9-ω-bromomethyl Ketone) with Diethylamine. 6 g acridylbromomethyl ketone is mixed with a solution of 9 ml diethylamine in 105 ml dry benzene. After an hour's boiling the initially pink solution is colored dark-red. After keeping for 40 days at room temperature, 4.5 g yellowish-green precipitate was obtained, consisting of a mixture of diethylamine hydrobromide and acridone (1.7 g). The benzene filtrate was evaporated to dryness in vacuum at 30-35°; the residue was dissolved in 20 ml cold methyl alcohol and filtered from the small amount of insoluble material, and 2.1 ml of 31% HBr solution in absolute alcohol was added to the filtrate. On standing, this solution deposited a small quantity of a substance which crystallized indefinitely and had decomposoition point 192-195°. It was not further investigated. The filtrate from this solid was fractionally precipitated with an alcoholic solution of picric acid. After removal of the initially separated resinous impurities, the picrate was recrystallized from methanol. Long, star-shaped clusters of dark needles with decomposition point 245-246°. A mixed test with the picrate of acridyl-9-(methyl ketone) does not give a depression.

Found %: C 56.63; H 3.40; N 12.32. $C_{21}H_{14}O_8N_4$. Calculated %: C 55.99; H 3.13; N 12.45.

SUMMARY

1. Treatment of 9-(diazoacetyl)-acridine with ammoniacal silver nitrate solution gives acridyl-9-acetamide. Hydrolysis of the latter with hydrochloric acid or alcoholic alkali gives 9-methylacridine as a result of decarboxylation of the intermediately formed acridyl-9-acetic acid. The action of a large excess of sodium nitrite on acridylacetamide in a mixture of sulfuric and acetic acids gives acridine-9-carboxylic acid.

2. Reaction of 9-(diazoacetyl)-acridine with glacial acetic acid in presence of copper acetate as catalyst gives acridyl-9-(acetoxymethyl ketone). This reaction could not be effected in the absence of a catalyst.

3. Reaction of acridyl-9-(ω-bromomethyl ketone) with piperidine gave a compound which could not be purified and whose analytical data were close to those calculated for acridyl-9-(piperidinomethyl ketone). Acridone and acridyl-9-(methyl ketone) were isolated in addition. Similarly the reaction of acridyl-9-(ω-bromomethyl ketone) with diethylamine gave acridone and acridyl-9-(methyl ketone).

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COPLANARITY OF THE NITRO GROUP WITH THE BENZENE RING AND ITS INFLUENCE ON THE COLOR OF DYES

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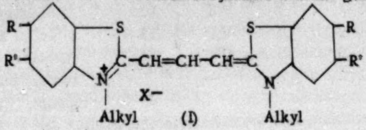
The influence of the nitro group on the color of organic dyes is bound up with its ability to repel electrons from the benzene ring and also from the conjugation chain of the dye. On displacement of the electrons from the benzene ring to the oxygen atoms of the nitro group, the bond between the nitrogen atom of the nitro group and the benzene ring acquires the character of a double bond. A necessary condition for such a displacement of electrons is the arrangement of the nitro group in the same plane as the benzene ring.* If a voluminous substituent is introduced in the ortho position to the nitro group. Its effect on light absorption must be reduced or entirely disappear, as actually occurs in ortho-substituted aromatic nitro compounds which absorb in the ultraviolet [2]. The influence of ortho-substituents on the auxochromic activity of the nitro group in the visible region has not been investigated. We undertook a study of this influence with reference to cyanine dyes and azo dyes.

For this purpose we synthesized a series of thiacarbocyanines with the general formula (I):



(I)

whose absorption maxima and molecular extinctions are set forth in Table 1 (dyes 1, 2, 4, 5 are listed for comparison).

TABLE 1

No. of dye	R	R'	Alkyl	λmax. in mμ	$\epsilon \cdot 10^{-4}$
1	H	H	C_2H_5	558	16.5
2	H	CH_3	C_2H_5	565	14.0
3	H	C_2H_5	CH_3	565	15.0
4	H	$C(CH_3)_3$	CH_3	565	14.4
5	NO_2	H	C_2H_5	584	13.7
6	NO_2	CH_3	C_2H_5	582	16.8
7	NO_2	C_2H_5	CH_3	580	16.9
8	NO_2	$C(CH_3)_3$	C_2H_5	570	16.3

The absorption curves of dyes 1, 4, 5, 6, 7, and 8 are plotted in Figure 1.

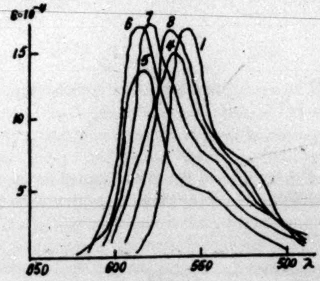


Figure 1

Introduction of a methyl group in the ortho-position to the nitro group (6) hardly changes the absorption curve. The ethyl group also has little effect on the color of the nitro dye (7). But the voluminous tertiary butyl group almost completely eliminates the auxochromic activity of the nitro group: the absorption maximum of dye 8 is shifted into the long-wave region by 5 mμ in comparison with dye 4 which does not contain a nitro group.

The same is observed with azo dyes. We synthesized three dyes with the general formula (II) and determined their absorption maxima and molecular extinctions (Table 2). The absorption curves of these compounds are plotted in Fig. 2.

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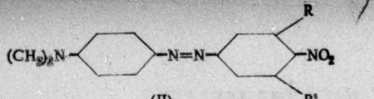
* This problem is considered in more detail in a paper by one of us on the coplanarity of the dimethylamino group with the benzene ring [1].



(II)

We see from Table 2 and Fig. 2 that one methyl group in the ortho-position to the nitro group has little effect on the absorption maximum and the shape of the absorption curve (10). The introduction of a methyl group in the second ortho-position, however, causes the maximum to shift by 32 $m\mu$ in the short-wave direction (11).

It is interesting that in both the cyanine and the azo dyes the introduction of substituents in the orthoposition to the nitro group mainly affects the absorption maximum of the dye and has little effect on the intensity of absorption.

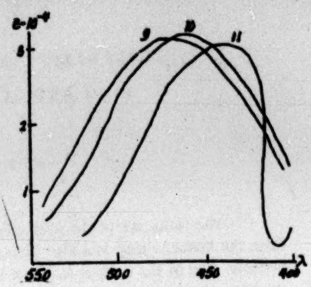


Figure 2

TABLE 2

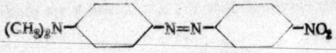
No. of dye	R	R'	$\lambda_{max.}$ (in $m\mu$)	$\epsilon \cdot 10^{-4}$
9	H	H	475	3.2
10	H	CH_3	460	3.2
11	CH_3	CH_3	443	3.1

TABLE 3

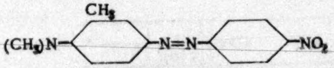
No. of dye	$\lambda_{max.}$ (in $m\mu$)	$\epsilon \cdot 10^{-4}$
9	475	3.2
12	438	2.2
13	418	3.5

In previous communications [3, 4], we showed that the methyl group has a strong influence on the auxochromic activity of the dimethylamino group. On the nitro group the methyl group has either no effect at all or a very weak one. An appreciable effect is manifested only by the tertiary butyl group or by two methyl groups. This was to be expected because the nitro group occupies a smaller volume than the dimethylamino group,* and is therefore exposed to a lesser degree to the action of the adjacent substituents.

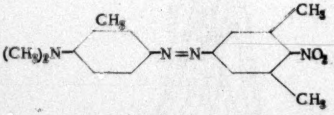
In Table 3 are set forth the absorption maxima and molecular extinctions of dyes 9, 12 and 13:



(9)



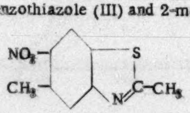
(12)



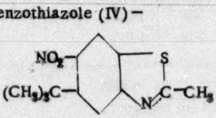
(13)

As was also to be expected, the least displacement of the maximum is observed in the case of dye 13 in which both of the auxochromes – the dimethylamino and the nitro group – are moved out of the plane of the molecule.

The synthesis of the bases required for the preparation of dyes with the general formula (I) – 2,5-dimethyl-6-nitrobenzothiazole (III) and 2-methyl-5-tert.butyl-6-nitrobenzothiazole (IV) –

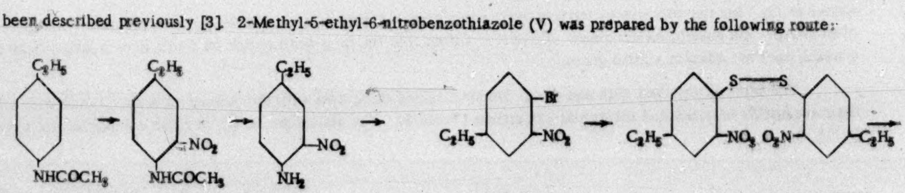


(III)



(IV)

has been described previously [3]. 2-Methyl-5-ethyl-6-nitrobenzothiazole (V) was prepared by the following route:



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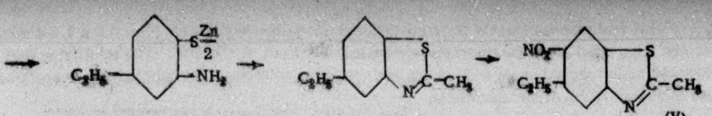
* The effective radius of the methyl group is 2A; that of the oxygen atom is 1.4A [5].



(V)

Nitration of 2-methyl-5-ethylbenzothiazole gives two nitro products: one with m.p. 100-102° and the second with m.p. 94-96°. The quaternary salt prepared from the nitro product with m.p. 100-102° gives with ethyl orthoformate a nitrothiacarbocyanine with an absorption maximum of 580 mμ, reduction of which with tin chloride gives an aminothiacarbocyanine with an absorption maximum of 590 mμ. On the basis of the considerations expounded in one of the previous papers [3], we assign structure (V) to the compound with m.p. 100-102°. The nitro product with m.p. 94-96° is probably 2-methyl-4-nitro-5-ethylbenzothiazole.

From the quaternary salts of bases (III to V) were prepared dyes 6, 7 and 8; from the quaternary salt of 2-methyl-5-ethylbenzothiazole was prepared dye 3.

EXPERIMENTAL

Intermediate Products

2-Methyl-5-ethylbenzothiazole. 33 g 3-nitro-4-bromoethylbenzene [6] was dissolved in 70 ml alcohol; addition was made of a hot mixture of 19 g crystalline sodium sulfite, 2.8 g sulfur and 20 ml alcohol. The mixture was boiled for 2 hours. 2,2'-Dinitro-4,4'-diethyldiphenyldisulfide came down in the form of an oil which later crystallized. Yield 21.5 g. 21.5 g disulfide was mixed with 120 ml glacial acetic acid. Gradual addition was made, with energetic stirring, of 42 g zinc dust and 90 ml conc. HCl. Stirring was continued for another hour; the solution was filtered, diluted with water and saturated with sodium acetate. The white precipitate of zinc mercaptide was filtered and dried. The 17.5 g of mercaptide was heated for 2 hours with an excess of acetic anhydride. Water was added to the solution; the mixture was gently heated for decomposition of the excess of acetic anhydride and made alkaline. The 2-methyl-5-ethylbenzothiazole separated in the form of an oil and was extracted with benzene and distilled in vacuum. Yield 10 g or 59%, calculated on the mercaptide.

Picrate: yellow needles (from alcohol), m.p. 165-167°.*

Found %: N 13.35, 13.51. $C_{10}H_{11}NS \cdot C_6H_3O_7N_3$. Calculated %: N 13.79.

Methiodide: colorless tablets (from alcohol), m.p. 199-201°.

Found %: I 39.95, 40.01. $C_{11}H_{14}NSI$. Calculated %: I 39.81.

2-Methyl-5-ethyl-6-nitrobenzothiazole (V). 6 g 2-methyl-5-ethylbenzothiazole was added dropwise with stirring to a mixture of 4.8 ml HNO_3 (s.g. 1.4) and 12 ml concentrated H_2SO_4. The mixture was then stirred for 20 minutes on the water bath and poured onto ice. The solidified nitroproduct was filtered, dissolved by heating in concentrated HCl and filtered from insoluble resinous impurities. The crystalline nitro product came down when the filtrate was diluted with water. Yield of crude product 4 g, m.p. 70-72°. Repeated crystallization from alcohol gave 0.9 g nitro product with m.p. 100-102°. The nitro product, isolated from the alcoholic mother liquor, was dissolved in concentrated HCl; the solution was diluted with double the amount of water and the precipitate was filtered; the product remaining in solution was separated by heavy dilution with water. By numerous repetitions of this procedure it was possible to resolve the product from the mother liquor into two fractions: with m.p. 100-102° (0.6 g) and with m.p. 94-96° (0.6 g). In this manner 1.5 g nitro product with m.p. 100-102° and 0.6 g with m.p. 94-96° were isolated. A mixture of both preparations melts at 74-76°. To the nitro product with m.p. 100-102° we assigned the structure of 2-methyl-5-ethyl-6-nitrobenzothiazole; to the nitro product with m.p. 94-96° the structure of 2-methyl-4-nitro-5-ethylbenzothiazole.

The 6-nitro isomer. Found %: N 12.83, 12.78. $C_{10}H_{10}O_2N_2S$. Calculated %: N 12.61.

Dyes

Bis-[3-methyl-5-ethylbenzothiazole (2)]-trimethinecyanine methiodide (3). 0.3 g 2-methyl-5-ethylbenzothiazole methiodide, 0.3 g ethyl orthoformate and 3 ml pyridine were boiled for 30 minutes. The precipitated dye (greenish needles) was filtered, washed with hot alcohol and dried. M.p. 280-282°. Yield 0.12 g or 50% of the theoretical.

Found %: I 24.07, 24.14. $C_{23}H_{25}N_2S_2I$. Calculated %: I 24.44

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* All the melting and boiling points in this paper have been corrected.

Bis-[3-ethyl-5-methyl-6-nitrobenzothiazole (2)]-trimethinecyanine-p-toluenesulfonate (6). 0.2 g 2,5-dimethyl-6-nitrobenzothiazole and 0.2 g ethyl p-toluenesulfonate were heated for 4 hours at 160-170°. The solidifying dark mass was dissolved in water and boiled several times with carbon until perfectly colorless. The solution was evaporated to dryness. Yield of salt 0.15 g or 42.5% of the theoretical.

0.1 g of the quaternary salt was boiled for 20 minutes with 0.1 g ethyl orthoformate in pyridine. The dye was precipitated by ether, filtered and recrystallized from alcohol. Green tablets with a metallic luster, m.p. 267-268° with decomposition. Yield 0.035 g or 47% of the theoretical.

Found %: N 8.40, 8.60. $C_{30}H_{30}O_4N_4S_3$. Calculated %: N 8.56.

Bis-[3-methyl-5-ethyl-6-nitrobenzothiazole (2)]-trimethinecyanine methosulfate (7). 0.2 g 2-methyl-5-ethyl-6-nitrobenzothiazole and 0.12 g dimethylsulfate were heated for 2 hours at 100°. The resultant methosulfate was boiled for 30 minutes in pyridine with 0.3 g ethyl orthoformate. The precipitated dye was filtered, washed with hot alcohol and dried. Yield 0.12 g (30%). Violet needles, m.p. above 300°.

Found %: N 9.26, 9.30. $C_{24}H_{26}N_4S_3$. Calculated %: N 9.43.

Bis-[3-ethyl-5-tert.butyl-6-nitrobenzothiazole (2)]-trimethinecyanine-p-toluene-sulfonate (8). 0.2 g 2-methyl-5-tert. butyl-6-nitrobenzothiazole and 0.2 g ethyl p-toluenesulfonate were heated for an hour to 150-160°. The formed crystals were washed with benzene and dried. Yield of quaternary salt 0.3 g or 75% of the theoretical. 0.2 g salt was boiled in pyridine with 0.2 g ethyl orthoformate for 20 minutes. The dye was precipiated with ether, filtered and recrystallized from alcohol. Green needles, m.p. 277° with decomposition. Yield 0.11 g or 69% of the theoretical.

Found %: N 7.45, 7.30. $C_{36}H_{42}O_7N_4S_3$. Calculated %: N 7.59.

4-Dimethylamino-3'-methyl-4'-nitroazobenzene. 0.4 g 3-methyl-4-nitroaniline [7] was diazotized and added to a cooled solution of 0.4 g dimethylaniline in dilute hydrochloric acid. After a few hours, the dye was filtered, dissolved with heating in strong HCl, filtered from insoluble impurities and precipitated with ammonia. Yield of crude dye 0.3 g (40%). Purification was effected by chromatography of benzene solution on alumina. After chromatography the dye was obtained in the crystalline state with m.p. 160°. It was recrystallized from benzene as brown needles, m.p. 160-162°.

Found %: N 19.84, 19.98. $C_{15}H_{16}O_2N_4$. Calculated %: N 19.72.

4-Dimethylamino-3',5'-dimethyl-4'-nitroazobenzene (11). 0.3 g 3,5-dimethyl-4-nitroaniline [8] was diazotized and added to a cooled solution of 0.3 g dimethylaniline in dilute HCl. After a few minutes addition was made of 2 g sodium acetate. The precipitated dye was filtered and crystallized from alcohol. Red needles, m.p. 176-178°. Yield 0.3 g or 50% of the theoretical.

Found %: N 18.89, 18.82. $C_{16}H_{18}O_2N_4$. Calculated %: N 18.79.

3,3',5'-Trimethyl-4dimethylamino-4'-nitrozobenzene (13). 0.3 g 3,5-dimethyl-4-nitroaniline was diazotized and added to a cooled mixture of 0.3 g dimethyl-o-toluidine, 5 ml alcohol and 2 g crystalline sodium acetate. The dye was filtered and crystallized from alcohol. Yield 0.25 g (40%). Orange needles, m.p. 112-114°.

Found %: N 18.02, 18.24. $C_{17}H_{20}O_2N_4$. Calculated %: N 17.95.

SUMMARY

1. A study was made of the effect of steric hindrance on the auxochromic activity of the nitrogroup in cyanine dyes and azo dyes containing nitro groups.

2. It was established that methyl and ethyl groups in the ortho-position to the nitro group weakly influence the absorption. The more voluminous tertiary butyl group almost completely suppresses the auxochromic activity of the nitro group. Two methyl groups in the ortho-position to the nitro group have an influence similar to that of the tertiary butyl group.

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INVESTIGATION OF THE ALKALOIDS OF *LEONTICE EWERSMANNII* BGE

I. A NEW ALKALOID TASPINE AND THE ALKALOID ISOLEONTINE. PREPARATION OF LEONTIDANE AND ISOLEONTANE

T. F. Platonova, A. D. Kuzovkov and P. S. Massagetov

"Leontik" or Lion's tail (*Leontice Ewersmannii* Bge) belongs to the family of the *Berberidacea* indigenous to Soviet Central Asia, Iran and Afghanistan. The presence of alkaloids in the plant was first established by P. S. Massagetov in 1926 [1]. The study of the alkaloids was commenced by A. P. Orekhov and R. A. Konovalova [2]. In 1932 they reported the isolation from the plant of three alkaloids: leontamine, leontidine, and a third substance in the form of its picrate with m.p. 178-180°. Of these three alkaloids, only the composition of leontamine was established, and the formula $C_{14}H_{26}N_2$ was assigned to it. The investigation was continued by S. Yu. Yunusov and L. G. Sorokina [3] who obtained a new alkaloid, leontine, with the composition $C_{15}H_{24}ON_2$; for leontidine they proposed the formula $C_{15}H_{20}ON_2$ and they obtained more accurate values for the constants of the base and its salts. The authors also isolated the alkaloids pachycarpine and lupanine from the plant.

The availability of the wild-growing lion's tail and its high content of organic bases prompted us to return to the study of the alkaloids of this plant. From the above-ground parts, gathered during the flowering period and containing a total of 0.77% alkaloids, we isolated leontidine (0.13%), pachycarpine (0.02%) and L-lupanine (0.003%). These alkaloids had previously been found in the plant. Fractional distillation in vacuum gave a base whose boiling and melting points were close to those of leontine and with the same composition. The melting point of the methoiodide and perchlorate also appeared to confirm the identity between our isolated base and leontine. This assumption had to be rejected, however, after our base was found to be optically active. Having been unable so far to establish whether this substance is an optically active form of leontine or a new alkaloid, we propose for it the name of isoleontine. The constants of leontine and isoleontine are compared in Table 1.

TABLE 1

	Base			Perchlorate	Methiodide	Picrate
	m.p.	b.p.*	$[\alpha]_D$	m.p.	m.p.	m.p.
Leontine $C_{15}H_{24}ON_2$	103-104°	195-205° (7 mm)	0°	232°	290-292°	—
Isoleontine $C_{15}H_{24}ON_2$	107-108	175-190 (3 mm)	-78.2	252	297	177-179°

* Boiling point of the fraction from which the base was isolated.

The specimen of the plant that we investigated contained 0.03% isoleontine. It should be noted that the melting point of isoleontine picrate agrees with that of the picrate prepared by Orekhov and Konovalova in the first investigation of the plant. Isoleontine was evidently also obtained for the first time by the cited authors in the form of its picrate.

In addition to the four bases mentioned above, we also isolated an alkaloid which differed markedly from the other alkaloids of this plant by virtue of the insolubility in water of the sulfate, hydrochloride and other salts with inorganic acids. The base* melts (with decomp.) 370°; the substance is insoluble in water and solutions of caustic alkalies, soluble in chloroform and dichloroethane; it is optically inactive. The composition of the base corresponds to the formula $C_{20}H_{19}O_6N$. The sulfate has the composition $C_{20}H_{19}O_6N \cdot 0.5H_2SO_4 \cdot H_2O$; it crystallizes from a large quantity of hot water (1:400) in the form of thin, white needles melting at 360°. The alkaloid contains two methoxyl, one methylenedioxy and two methyl groups linked to nitrogen. It forms a crystalline methoiodide $C_{20}H_{19}O_6N \cdot CH_3I \cdot H_2O$. The nitrogen atom is evidently tertiary and in an open chain. All of the stated properties show that the alkaloid is a new one, and we therefore propose for it the name of taspine (from the Uzbek name "taspi" for lion's tail). Alkaline hydrolysis of taspine gave an amino acid with the composition $C_{20}H_{21}O_7N \cdot H_2O$. Its formation, not involving a change in the number of carbon atoms in the molecule, points to the presence of a lactone group, and this is confirmed by transformation of the amino acid into taspine sulfate when heated with dilute sulfuric acid. On the basis of the whole of the foregoing data, the formula of taspine may be written out in the following form $C_{14}H_5(OCH_3)_2(CH_2O_2)(COO)N(CH_3)_2$.

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* Crystallized from toluene; form — light yellow needles.

In approaching the investigation of the structure of the alkaloids isoleontine and leontidine, we decided that we must start by establishing the character of the oxygen-free, saturated heterocyclic substances forming the basis of these alkaloids, and we therefore aimed at securing experimental data that would confirm or disprove the statement [3] that the basis of the alkaloids of lion's tail is the pachycarpine nucleus, and that these alkaloids differ from each other in respect to the arrangement of the carbonyl group, to the presence of double bonds and to the spatial structure. In order to obtain such an oxygen-free saturated compound from leontidine, it was necessary to reduce the carbonyl group and the two double bonds; this was accomplished by catalytic reduction of the alkaloid with platinum catalyst in a hydrochloric acid medium in conditions similar to those for the reduction of the alkaloid thermopsine to α-isosparteine [4].

We worked with leontidine with m.p. 118-119° and $[\alpha]_D$ −192.2°, prepared from the hydrochloride with m.p. 293°. These constants are in accord with those in the literature. Reduction of leontidine was accompanied by absorption of 4.2 moles hydrogen. A liquid, optically active base was obtained which formed well-crystallized salts: monohydroiodide, sulfate, dihydroiodide, perchlorate. The substance does not contain primary or secondary nitrogen atoms and does not change under the action of nitrous acid. Numerous analyses of the base and its salts showed that its composition corresponds to the formula $C_{14}H_{24}N_2$ and not to $C_{15}H_{26}N_2$ as would have been expected on the assumption that the formula of leontidine was $C_{15}H_{20}ON_2$. In spite of the closeness of the analytical values for the possible formulas, the analyses show conclusively that leontidine has a composition corresponding to the formula $C_{14}H_{18}ON_2$. All the analytical data are set forth in Table 2. We see from this table that not one of the results of analysis contradicts the formula $C_{14}H_{18}ON_2$ for leontidine or the formula $C_{14}H_{24}N_2$ for the product of its hydrogenation, apart from which a series of analyses is inconsistent with the formulas $C_{15}H_{20}ON_2$ and $C_{15}H_{26}N_2$.

Consequently leontidine cannot be a member of the sparteine group of alkaloids: the oxygen-free saturated substance on which it is based, for which we propose the name leontidane, is a homolog of sparteine and differs from the latter at the methlene group. It may be suggested that the molecule of leontidane contains 3 six-membered rings and one five-membered ring. We suggest that the establishment of the composition $C_{14}H_{18}ON_2$ for leontidine once more throws doubt on the hypotheses (based only on analogy) of some investigators [3] that leontamine must, in consequence of its occurrence jointly with pachycarpine, possess the composition $C_{15}H_{26}N_2$ and not $C_{14}H_{26}N_2$ as was established by A. P. Orekhov and R. A. Konovalova.

For the purpose of obtaining the oxygen-free, saturated skeleton of isoleontine, it was necessary to reduce the carbonyl group to methylene. Our experiments showed that this is easily accomplished by catalytic reduction of isoleontine with platinum catalyst in a hydrochloric acid medium. Apart from the above-mentioned reduction of the carbonyl group of thermopsine, the literature contains other examples of catalytic reduction of carbonyl groups to methylenes [5]. We were unable, however, to find any examples of reduction by this method of carbonyl groups in saturated compounds Catalytic reduction of isoleontine with platinum catalyst in a hydrochloric acid medium resulted in absorption of 1.9 moles hydrogen. A crystalline, optically active base was obtained which did not contain secondary nitrogen atoms. The substance differs from known compounds of the same composition and we therefore propose for it the name of isoleontane. Isoleontane is an isomer of sparteine; it remains for further research to decide whether the difference between these compounds depends on stereoisomerism or on a more profound structural difference.

EXPERIMENTAL

146 kg air-dry, pulverized, above-ground parts of the plant were wetted with 10% ammonia solution and exhaustively extracted with dichloroethane. The dichloroethane solution was shaken with 15% sulfuric acid solution. Taspine sulfate came down in the form of a grey precipitate. This was filtered, washed with water and crystallized from 10% aqueous acetic acid (1:150). The first crystallization gave 268 g taspine sulfate (0.18% of the weight of the plant) and the second crystallization gave 233 g. The filtered acid extract (after separation of the taspine sulfate), with ice cooling, was made alkaline with 25% ammonia solution and exhaustively extracted with chloroform. The chloroform was driven off, leaving a residue of 830 g total bases (0.56% of the weight of the plant) in the form of a dark-brown oil.

TABLE 2

Leontidine base					Product of hydrogenation of leontidine				
					Base				Hydroiodide
	C	H	N	M		C	H	N	I
$C_{15}H_{20}ON_2$ Calculated %	73.71	8.29	11.46	244.4	$C_{15}H_{26}N_2$ Calculated %	76.85	11.18	11.95	51.78
$C_{14}H_{18}ON_2$ Calculated %	73.04	7.88	12.17	230.02	$C_{14}H_{24}N_2$ Calculated %	76.32	10.98	12.72	53.3
Found %	72.73, 73.12, 72.62	7.71, 7.92, 8.11	11.82, 11.78,	231.4, 229.8,	Found %	75.91, 75.91, 75.67, 75.56	11.02, 10.88, 10.56, 10.92	13.04, 12.96, 13.12	53.84, 53.95

Isolation of the alkaloids. 830 g total alkaloids was dissolved in 500 ml acetone and acidified with an alcoholic solution of HCl until weakly acid to congo. The crystalline hydrochloride of leontidine (270 g) was thus precipitated. Crystallization from alcohol gave 198 g leontidine hydrochloride with a light-yellow color, m.p. 293°. The organic solvent was distilled off from the hydrochloric acid mother liquors after precipitation and crystallization of leontidine hydrochloride, and then the total bases were separated (500 g). These total alkaloids were subjected to fractional distillation in vacuum at 3 mm; three repetitions of this process gave the following fractions: 1) b.p. 120-150° (35.5g), a light-brown oil; 2) b.p. 171-174° (26 g), a yellow oil; 3) b.p. 175-190° (126 g), a light-yellow oil; 4) b.p. 191-215° (43 g), a viscous, greenish-yellow oil.

The first fraction was once again subjected to vacuum distillation. Two fractions were collected at 8 mm: 3 g with b.p. 126-135° and 28 g with b.p. 136-159°. From the second fraction was obtained a monohydroiodide by dissolving in 5% sulfuric acid solution and adding to the solution (neutral to bromothymol blue) a saturated solution of KI. The precipitated salt, after crystallization from water, melted at 233-234° and did not give a depression with pachycarpine monohydroiodide.

The second fraction was converted into a monohydroiodide by the same procedure as above. Yield 7.9 g salt with m.p. 189-190° (after two crystallizations from water) and $[\alpha]_D$ −44.4°. These constants agree with the constants of L-lupanine monohydroiodide. Further confirmation was obtained by preparing the base and the perchlorate whose constants agreed with those of lupanine base and its perchlorate. Base: an optically active, crystalline substance, $[\alpha]_D$ −80.70°. The perchlorate has m.p. 212-213°, $[\alpha]_D$ −47.8°. Found %: C 51.05, 51.09; H 6.77, 7.10, N 8.26, 8.03. $C_{15}H_{24}ON_2 \cdot HClO_4$. Calculated %: C 51.65; H 7.22; N 8.03. From the mother liquors, following separation of L-lupanine hydrochloride, no other pure substances could be separated.

The 3rd fraction was dissolved in 200 ml acetone. To the solution was added a saturated alcoholic solution of picric acid until the reaction was acid. Crystalline isoleontine picrate came down and was filtered off and extracted with boiling acetone (twice with 150 ml each time). Yield 75 g finely crystalline powder with m.p. 177-179°. No other pure alkaloids could be isolated from the mother liquors following separation of isoleontine picrate.

The fourth fraction was dissolved in 100 ml acetone. To the solution was gradually added alcoholic HCl until acid to congo. A white crystalline precipitate of a hydrochloride was thus obtained (31.7 g). M.p. (from alcohol) 310-311°. No depression in admixture with leontidine hydrochloride.

Preparation of taspine. After recrystallization from hot water (1:400), taspine sulfate was in the form of thin, white needles which charred at above 360°.

3.110 mg substance: 6.334 mg CO_2; 1.481 mg H_2O. 3.808 mg substance: 7.731 mg CO_2; 1.770 mg H_2O. 8.320 mg substance: 0.241 ml N_2 (24.5°, 728 mm). 8.205 mg substance: 0.255 ml N_2 (25.5°, 727 mm). 8.275 mg substance: 0.266 ml N_2 (23.5°, 727 mm). 5.325 mg substance: 1.520 mg $BaSO_4$ (Carius). 16.560 mg substance: 2.06 ml 0.01 N $Na_2S_2O_3$ (Gelman). Found %: C 55.55, 55.37; H 5.33, 5.20; N 3.18, 3.39, 3.01; S 3.92, 3.99. $C_{20}H_{19}O_6N \cdot 0.5H_2SO_4 \cdot H_2O$. Calculated %: C 55.04; H 5.08; N 3.20; S 3.67.

230 mg taspine sulfate was mixed with 200 ml 10% ammonia solution and the base exhaustively extracted with chloroform. After distilling off the solvent to a small volume, acetone was added to the residue. The base came down in the form of fine, white needles which quickly yellowed. Yield 175 g taspine base (0.12% of the weight of the plant). After crystallization from toluene, the base melted at 370°. Taspine is insoluble in water, solutions of caustic alkali and ammonia, alcohol or acetone; it dissolves in chloroform and dichloroethane. The salts with inorganic acids have extraordinarily poor solubility in water. The alkaloid is optically inactive.

3.016 mg substance: 7.171 mg CO_2; 1.346 mg H_2O. 3.809mg substance: 9.103 mg CO_2; 1.736 mg H_2O. 3.689 mg substance: 8.788 mg CO_2; 1.668 mg H_2O. 6.050 mg substance: 0.213 ml N_2 (24°, 736 mm). 7.385 mg substance: 0.243 ml N_2 (21°, 738 mm). 9.000 mg substance: 0.318 ml N_2 (25.5°, 727 mm). 9.435 mg substance: 15.10 ml 0.02 N, $Na_2S_2O_3$. 8.555 mg substance: 13.78 ml 0.02 N $Na_2S_2O_3$. 7.897 mg substance: 12.54 ml 0.02 N $Na_2S_2O_3$. Found %: C 64.85, 65.17, 64.97; H 4.99, 5.10, 5.06; N 3.92, 3.72, 3.86; OCH_3 16.78, 16.66; $N(CH_3)_2$ 11.82. $C_{20}H_{19}O_6N$. Calculated %: C 65.04; H 5.18; N 3.79; $2OCH_3$ 16.80; $N(CH_3)_2$ 11.92.

Taspine methoiodide. 0.5 g taspine, 20 ml methanol and 1 ml methyl iodide were boiled on a water bath for 4 hours. During this period the solid changed from light and voluminous to heavy and dense. Crystallization from water (1:750) gave 0.59 g methiodide in the form of colorless, small needles.

3.815 mg substance: 6.696 mg CO_2; 1.715 mg H_2O. 3.481 mg substance: 6.105 mg CO_2; 1.500 mg H_2O. 7.000 mg substance: 0.163 ml N_2 (24°, 728.5 mm). 5.202 mg substance: 6.0 ml 0.02 N $Na_2S_2O_3$. 5.202 mg substance: 7.98 ml 0.02 N $Na_2S_2O_3$. Found %: C 47.87, 47.83; H 5.03, 4.82; N 2.57, OCH_3 11.92; $N(CH_3)_2$ 11.4. $C_{20}H_{19}O_6N \cdot CH_3I \cdot H_2O$. Calculated %: C 47.65; H 4.57; N 2.64; $2OCH_3$ 11.82; $N(CH_3)_2$ 11.15.

Alkaline hydrolysis of taspine. 0.4 g taspine base was boiled for 15 minutes with 70 ml 0.1 N NaOH solution; the base gradually went into solution. Acidification of the cooled solution with sulfuric acid until the reaction was acid to congo resulted in precipitation of fine white crystals of amino acid. The precipitate was filtered off, crystallized from 5% acetic acid solution and dried in vacuum (8 mm) at 83°. The substance was soluble in solutions of caustic alkali and ammonia and was not extracted from these solutions by organic solvents and was not brought down by saturated carbon dioxide solution.

3.159 mg substance: 6.862 mg CO_2; 1.614 mg H_2O. 4.122 mg substance: 8.900 mg CO_2; 2.247 mg H_2O. 6.340 mg substance: 0.196 ml N_2 (22°, 736 mm). Found %: C 59.24, 58.89; H 5.72, 6.10; N 3.46. $C_{20}H_{21}O_7N \cdot H_2O$. Calculated %: C 59.26; H 5.71; N 3.45.

The substance went into solution when heated with 10% sulfuric acid solution; on further heating and boiling, taspine sulfate was precipitated; insoluble in solutions of caustic alkalies and ammonia. The taspine sulfate was mixed with 10% ammonia solution and the base was extracted with chloroform. The chloroform was driven off and the base recrystallized from toluene.

Found %; C 65.22, 65.03; H 5.41, 5.36; N 4.02, 3.87. $C_{20}H_{19}O_6N$. Calculated %: C 65.04; H 5.18; N 3.79.

Preparation of leontidine. 198 g leontidine hydrochloride was dissolved in a small quantity of water. The solution was made alkaline with 40% NaOH solution and the base repeatedly extracted with ether. The ethereal extract was dried with anhydrous sodium sulfate and the solvent completely removed. The residue was 132 g viscous, light-yellow oil which crystallized on standing. After two recrystallizations from a mixture of benzene and ether (1:4), leontidine base melted at 118-119°.

0.1737 g substance: 10 ml methyl alcohol; l 1 dm; α_D −3.34°; $[\alpha]_D$ −192.2°. 3.107 mg substance: 8.281 mg CO_2; 2.142 mg H_2O. 3.998 mg substance: 10.639 mg CO_2; 2.900 mg H_2O. 4.745 mg substance: 0.490 ml N_2 (21°, 749 mm). 4.728 mg substance: 0.498 ml N_2 (23°, 734 mm). 0.4234 mg substance: 18.29 ml 0.1 N HCl (methyl red). 0.4299 mg substance: 18.70 ml 0.1 N HCl(methyl red). Found %: C 72.73, 72.62; H 7.71, 8.11; N 11.82, 11.73; equiv. 231.4, 229.8. $C_{14}H_{18}ON_2$. Calculated %: C 73.04; H 7.88; N 12.17; equiv. 230.2.

Leontidine hydrochloride. A crystalline precipitate was formed on mixing alcoholic solutions of leontidine and hydrochloric acid. M.p. of hydrochloride 310-311° (after recrystallization from alcohol).

3.743 mg substance: 8.163 mg CO_2; 2.541 mg H_2O. 3.923 mg substance: 8.557 mg CO_2; 2.669 mg H_2O. 5.146 mg substance: 0.450 ml N_2 (23°, 734 mm). 8.169 mg substance: 5.85 ml 0.01 N H_2SO_4 (Kjeldahl). 7.854 mg substance: 3.966 ml 0.1 N $AgNO_3$. 7.460 mg substance: 3.847 ml 0.1 N $AgNO_3$. Found %: C 59.51, 59.52; H 7.60, 7.61; N 9.74; 10.02; Cl 12.48, 12.75. $C_{14}H_{18}ON_2$ $HCl \cdot H_2O$ Calculated %: C 59.04; H 7.43; N 9.84; Cl 12.45.

Preparation of isoleontine. 62 g isoleontine picrate was treated with an 18% solution of HCl. The separated picric acid was filtered off and washed with dilute hydrochloric acid. The filtrate and the wash liquor were extracted with ether until the whole of the picric acid was removed. The acid solution was cooled with ice, made alkaline with 40% NaOH solution and exhaustively extracted with ether. The ethereal extract was dried with anhydrous sodium sulfate and evaporated down to a small volume. Crystalline isoleontine came down (24.3 g). Two crystallizations from ether gave 20 g isoleontine in the form of small, colorless crystalline needles with m.p. 107-108°.

0.4318 g subs.: 3.1 ml abs. alcohol; $\underline{1}$ 0.5 dm; α_D −5.45°; $[\alpha]_D$ − 78.2°.

3.940 mg substance: 10.458 mg CO_2; 3.350 mg H_2O. 4.062 mg substance: 10.810 mg CO_2; 3.422 mg H_2O. 5.338 mg substance: 0.517 ml N_2 (21.5°, 734 mm). 5.327 mg substance: 0.517 ml N_2 (21.5°, 734 mm). Found %: C 72.44, 72.62; H 9.51, 9.43; N 10.83, 10.85. $C_{15}H_{24}ON_2$. Calculated %: C 72.55; H 9.74; N 11.28.

Isoleontine base is easily soluble in water and in all common organic solvents except hexane and ligroine.

Isoleontine perchlorate was prepared by adding a saturated aqueous solution of magnesium perchlorate to a solution of isoleontine in 5% HCl. After recrystallization from water it melted at 252° (with decomposition).

3.405 mg substance: 0.249 ml N_2 (20°, 742 mm). 6.023 mg substance: 0.422 mg N_2 (18°, 742 mm).
Found %: N 8.32, 8.02; $C_{15}H_{24}ON_2 \cdot HClO_4$. Calculated %: N 8.03.

Isoleontine methiodide. To a solution of isoleontine in acetone was added methyl iodide. Crystalline isoleontine methiodide came down on standing. After crystallization from alcohol (1:3) it melted at 297° (with decomposition).

4.035 mg substance: 6.33 ml 0.01 N $Na_2S_2O_3$. 3.944 mg substance: 6.06 ml 0.01 N $Na_2S_2O_3$. Found %: I 33.20, 32.51. $C_{15}H_{24}ON_2 \cdot CH_3I$. Calculated %: I 32.51.

Hydrogenation of leontidine. 6 g leontidine with m.p. 118-119° was dissolved in 360 ml 1 N HCl; to the solution was added 2.27 g platinum oxide and the whole shaken in a hydrogen atmosphere under a small pressure. After $2\frac{1}{2}$ hours, 2.5 liters hydrogen had been absorbed (4.2 moles), and the absorption was concluded. The catalyst was thereupon filtered off and the solution made alkaline with 40% NaOH solution and exhaustively extracted with ether. The ethereal extract was dried with anhydrous sodium sulfate and the solvent completely driven off. The residue of 5.6 g light-yellow oil was neutralized with 5% sulfuric acid solution (bromothymol blue indicator), the solution was filtered and to the filtrate was added a saturated solution of KI. The crystalline monohydroiodide immediately came down (4.6 g). Recrystallization from water gave 4.1 g of a white, lustrous crystalline powder which melted at 219-220°.

0.1858 g substance: 3 ml alcohol; $\underline{1}$ 0.5 dm; α_D + 0.32°; $[\alpha]_D$ + 10.33°.

Leontidane base. 3.8 g of the monohydroiodide was dissolved in water and excess of 40% NaOH was added. The alkaline solution was exhaustively extracted with ether, the ethereal extract was dried with anhydrous sodium sulfate, and the ether completely driven off to leave 2.5 g of liquid leontidane base. This distils in vacuum at 141-144° (5 mm). The base dissolves readily in all the common organic solvents.

$\underline{1}$ 0.5 dm; α_D −3.88°; $[\alpha]_D$ −7.76° (without solvent). 0.3028 g subs.: 5 ml alcohol, $\underline{1}$ 0.5 dm; α_D + 0.5°; $[\alpha]_D$ + 16.5°.

3.596 mg subs.: 10.002 mg CO_2; 3.543 mg H_2O. 4.332 mg subs.: 12.051 mg CO_2; 4.212 mg H_2O. 6.308 mg subs.: 0.729 ml N_2 (21°, 734 mm). 6.537 mg subs.: 0.765 ml N_2 (21°, 734 mm). Found %: C 75.91, 75.91; H 11.02, 10.88; N 12.96, 13.12. $C_{14}H_{24}N_2$. Calculated %: C 76.32; H 10.98; N 12.72.

Leontidane sulfate. 0.5 g base was dissolved in 1 ml absolute alcohol and 10% sulfuric acid solution in absolute alcohol was added until the reaction was acid to congo. Addition of a small amount of acetone brought down white crystals which deliquesced in the air. M.p. 229-230°.

0.1538 g subs.: 3 ml alcohol; $\underline{1}$ 0.5 dm; α_D + 0.5.; $[\alpha]_D$ + 19.5°.

Leontidane dihydroiodide. Mixing of alcoholic solutions of the base and hydriodic acid (acid reaction to congo) caused a crystalline precipitate to appear. After crystallization from alcohol, the salt melted at 268° (with decomposition).

4.802 mg substance: 12.22 ml 0.02 N $Na_2S_2O_3$. 3.200 mg substance: 8.16 ml 0.02 N $Na_2S_2O_3$.
Found %: I 53.84, 53.95. $C_{14}H_{24}N_2 \cdot 2HI$. Calculated %: I 53.3.

Leontidane perchlorate was prepared by adding magnesium perchlorate to a solution of the base in 5% sulfuric acid. M.p. (from 90% alcohol) 234°.

0.1547 g subs.: 3 ml water; 1 0.5 dm; α_D + 0.53°; $[\alpha]_D$ + 20.55°.

5.201 mg subs.: 0.283 ml N_2 (17.5°, 734 mm). 5.139 mg subs.: 0.295 ml N_2 (18°, 733 mm).
Found %: N 6.18, 6.49; $C_{14}H_{24}N_2 \cdot 2HClO_4$. Calculated %: N 6.67.

Hydrogenation of isoleontine. 1.8 g isoleontine (m.p. 107-108°) was dissolved in 100 ml 1 N HCl solution and 0.86 g platinum oxide was added. On shaking in a hydrogen atmosphere for 14 hours, 310 ml (1.9 moles) hydrogen was taken up. At the termination of hydrogenation the catalyst was filtered off and the solution made alkaline with 40% NaOH solution and exhaustively extracted with ether. The extract was dried with solid KOH and the solvent driven off to leave 1.65 g yellowish crystals with m.p. 68-72°. After two crystallizations from ether (1:3) the base melted at 77-78.5°. Readily soluble in water and alcohol, less soluble in ether and acetone.
0.1634 g subs.: 3.05 ml abs. alcohol: 1 0.5 dm; α_D −0.81°; $[\alpha]_D$ −30.1°.

4.091 mg subs.: 11.559 mg CO_2; 4.001 mg H_2O. 3.709 mg subs.: 10.453 mg CO_2 3.699 mg H_2O.
4.830 mg subs.: 0.487 ml N_2 (23°, 748 mm). 4.865 mg subs.: 0.500 ml N_2 (23.5°, 732 mm).
Found %: C 77.11, 76.91; H 10.94, 11.15; N 11.44, 11.40. $C_{15}H_{26}N_2$. Calculated %: C 76.85; H 11.19; N 11.95.

Isoleontane picrate was prepared by mixing alcoholic solutions of the base and picric acid. M.p. 256° (with decomp.) after crystallization from 1:1 alcohol-acetone.

Isoleontane hydrochloride. Prepared in the form of slender needles by adding alcoholic HCl to an alcoholic solution of the base until the reaction was acid to congo. After crystallization from acetone-alcohol (1:1 mixture) and drying at 105°, the hydrochloride melted at 368° with considerable sublimation.

0.1709 mg subs.: 3 ml alcohol; 1 0.5 dm; α_D −0.42°; $[\alpha]_D$ −14.7°; 3.860 mg subs.: 7.959 mg CO_2; 3.291 mg H_2O; 4.358 mg subs.: 8.943 mg CO_2; 3.619 mg H_2O. 4.389 mg subs.: 0.342 ml N_2 (22°, 733 mm). 6.351 mg subs.: 0.488 ml N_2 (22°, 733 mm). 7.630 mg subs.: 6.817 ml 0.1 N $AgNO_3$. 7.945 mg subs.: 6.955 ml 0.1 N $AgNO_3$.
Found %: C 56.27, 56.00; H 9.54, 9.29; N 8.70, 8.58; Cl 22.10, 21.66. $C_{15}H_{26}N_2 \cdot 2HCl \cdot H_2O$. Calculated %: C 55.38; H 9.29; N 8.61; Cl 21.80.

Isoleontane methiodide. To a solution of the base in acetone was added MeI. On standing, a crystalline precipitate appeared which melted (from 75% alcohol) at 292° (with decomp.).

0.1093 g subs.: 2.9 ml water; 1 0.5 dm; α_D −0.1°; $[\alpha]_D$ −5.3°.

SUMMARY

1. A new alkaloid with the composition $C_{20}H_{19}O_6N$, named taspine, was isolated from Leontice Ewersmannii Bge.

2. An alkaloid $C_{15}H_{24}ON_2$ was isolated which differs from leontine in optical activity and was named isoleontine.

3. The alkaloid leontidine was found to have the composition $C_{14}H_{18}ON_2$ and not $C_{15}H_{20}ON_2$.

4. From leontidine $C_{14}H_{18}ON_2$ and isoleontine $C_{15}H_{24}ON_2$ were prepared the hydrogen-free saturated compounds leontidane $C_{14}H_{24}N_2$ and isoleontane $C_{15}H_{26}N_2$.

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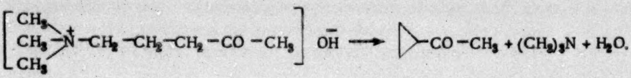
SYNTHESIS OF METHYLCYCLOPROPYL KETONE BY EXHAUSTIVE METHYLATION

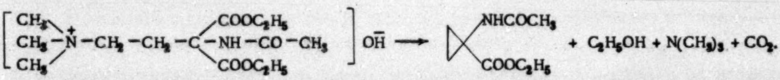
Ya. M. Slobodin and N. A. Selezneva

The method developed by Vagner [1] for preparation of methylcyclopropyl ketone consists, as we know, of cleavage of hydrogen bromide from acetopropyl bromide by the action of caustic alkali. Due to the high mobility of the hydrogen of the methylene group in the α-position to the carbonyl, cleavage of hydrogen bromide is accompanied by closure of the three-membered ring. This reaction was later improved [2,3] and the yield of methylcyclopropyl ketone was made nearly quantitative.

It may be suggested that decomposition of a quaternary ammonium base containing the trimethylammonium group in the γ-position to the carbonyl would, thanks to the high mobility of the hydrogens of the methylene group adjacent to the carbonyl, likewise proceed with closure of the three-membered ring



Only one investigation [4] is mentioned in the literature in which it is shown that decomposition of a quaternary ammonium base with formation of a compound with the cyclopropane ring is possible. The authors in question accomplished the reaction



In the present investigation we studied the decomposition of the hydroxide of 1-trimethylammonium-pentan-4-one. The decomposition gave the ketone in a yield of 40-45% of the theoretical.

B.p 111-111.5°; d_4^{20} 0.8947; n_D^{20} 1.4220; MR_D 23.76.

C_5H_8O. Calculated: MR_D 23.80 (increment of the three-membered ring assumed to be 0.7).

The 2,4-dinitrophenylhydrazone of the ketone melted at 136-138°. A mixture with the 2,4-dinitrophenylhydrazone prepared from pure methylcyclopropyl ketone melted without depression (137-138°).

The Raman spectrum of the prepared ketone was completely identical with the spectrum of methylcyclopropyl ketone [3].

The starting acetopropyl bromide was prepared by the action of hydrogen bromide on acetopropyl alcohol [5]. Treatment of the bromide with a small excess of trimethylamine in the cold converted it into trimethylammonium-pentanone bromide. Distillation was performed by slow distillation of the salt with a small excess of 40% KOH solution. The products of decomposition were acidified with dilute sulfuric acid. The ketone was extracted with ether and dried; the ether was driven off and the residue twice distilled from a flask with a column.

It should be noted that the yields of ketone were negligibly small by decomposition of the free ammonium base obtained by the action of silver oxide on the salt.

SUMMARY

Methylcyclopropyl ketone was prepared by distillation of a salt of 1-trimethylammonium-pentan-4-one with caustic alkali.

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SECONDARY PERIODICITY IN THE D. I. MENDELEEV TABLE OF ELEMENTS

V. P. Shishokin

In chemical texts it is usually stated that the properties of elements, arranged vertically in the D. I. Mendeleev Table, change successively. However, even in 1887, A. I. Bazarov [1] showed that a periodic change of the value of the atomic weights of elements occurs in groups of the Mendeleev Table. In order to obtain a better representation, Bazarov compared not the atomic weights, but the ratio of the atomic weights of the elements arranged side by side. Thomson showed by the determination of the heats of formation, conducted at the end of the nineteenth century and the beginning of the twentieth, that a greater affinity for oxygen was found for Cl and I, S and Te, P and Sb, than for Br, Se, and As, respectively.

The periodic changes of several properties in the groups of the Mendeleev Table were examined by E. V. Biron in 1915 in the publication, "Appearance of Secondary Periodicity" [2]. The appearance of secondary periodicity was observed in the properties of oxygen compounds (oxides, acids, and salts) of elements of the main sub-groups in groups IV - VII. In group III, the secondary periodicity is manifested less acutely, while, in groups I and II, it is scarcely apparent. Secondary periodicity is not found in the properties of hydrogen compounds.

Later, experimental investigations by Roth [3] confirmed the appearance of secondary periodicity in the change of the heats of formation of oxides in the main subgroups of groups IV - VII.

E. V. Biron's paper passed unnoticed by Russian and foreign investigators. Thus, A. M. Berkenheim [4] in his paper on the relation of the heat of formation of chemical compounds with the position of the elements in the Mendeleev Table, did not recognize the appearance of secondary periodicity, which explains the deviation of the calculated values from the experimental results.

Bazarov's paper showed the periodic change of atomic weights of elements even in the periodic table itself. The latter case is a special form of secondary periodicity subordinate to the main periodicity of the Mendeleev Table.

The present text is aimed at giving supplementary material on the periodic relationship between properties and positions of elements in the Mendeleev Table and to relate these to changes in the values of the ionization potential.

Fig. 1 gives the difference of the square roots of the eighth and first ionization potential ($\sqrt{I_8} - \sqrt{I_1}$) on the vertical axis in relation to the atomic number of the element, which is proportional to the tangent of the angle of inclination of the lines expressing Moseley's Law by means of ionization potential values (the latter are proportional to the vibration frequency). The ionization potential values are taken from Kei and Lebi's "Handbook for the Physical Investigator" [5]. The curve shows the presence of maxima for He, Ne, Ni, Pd and Pt, which corresponds to the distribution of elements in the Mendeleev Table in the following periods: H - He, Li - Ne, Na - Ni, Cu - Pd, Ag - Pt; the last period is begun by gold. The first two periods coincide with those of the Mendeleev Table, the final four do not. Therefore it must be concluded that the position of the elements in the Mendeleev Table is not immutable (this view was previously expressed by S. A. Shchukarev).

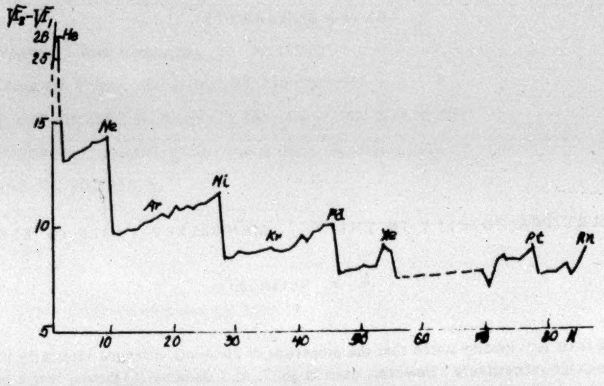

Fig. 1. Curve of the relation of the difference between the square roots of the eighth and first ionization potentials to the atomic number of the elements.

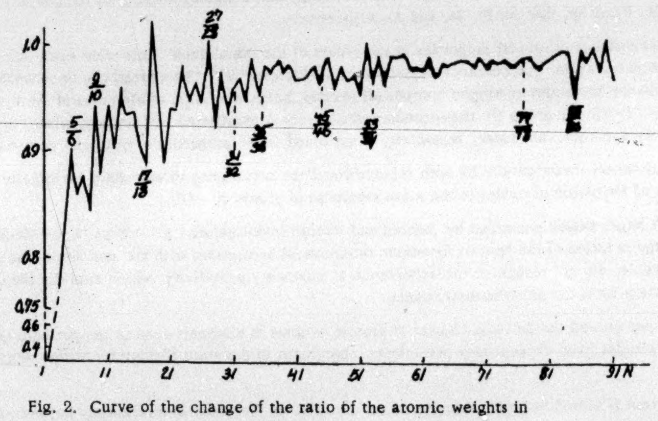

Fig. 2. Curve of the change of the ratio of the atomic weights in relation to the atomic number of the elements.

By supplementing Bazarov's diagrams with modern data which show the relation between atomic weights and atomic number of the element (in a horizontal direction on the Mendeleev Table), points corresponding to the relation of the atomic weights of gallium and germanium were of special value; up to this point, the maxima corresponded to the ratio of the atomic weights of the odd element to the even; after this point, the maxima corresponded to the ratio of the even element to the odd (Fig. 2).

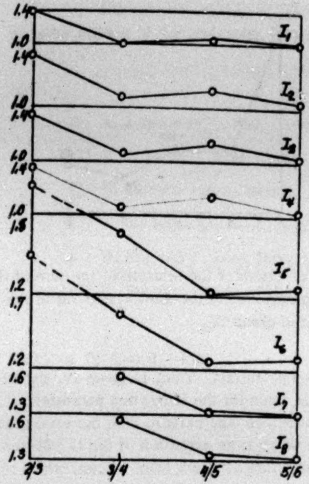

Fig. 3. Curve of the change of ionization potential for elements of the main subgroups of group IV.

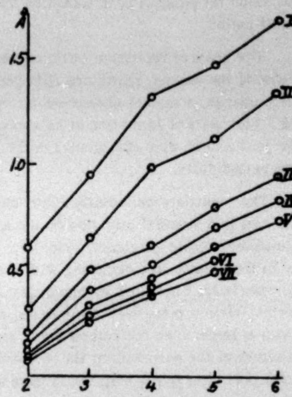

Fig. 4. Curve of the change of size of the crystals of positive ions in relation to the period number for elements of the main subgroup.

Fig. 3 gives the change of the ionization potentials (from the first to the eighth) for elements of the main subgroups of group IV, where the ratio of the ionization potential of the element (upper to the lower) is represented by the vertical axis, and the above corresponding periods by the horizontal. Periodicity is found in the change of the ionization potential only of the first second, third, and fourth potentials, i.e., it does not exceed the group number, wherein it becomes more distinct with the increase in the potential number (the periodicity is very weakly expressed for the fifth potential and is absent for the sixth, seventh and eighth). The same relationship holds for other groups of the Mendeleev Table (for the inert elements the periodicity is shown by all eight potentials; the ninth potential, calculated by means of extrapolation, does not show periodicity). By placing hydrogen in group I, as well as in group VII, a periodic change of the first ionization potential occurs.

In all groups a periodic change of the atomic number (ratio of atomic numbers) of the elements of the main subgroups occurs; it appears less distinct (in gradual form) for groups III and IV. Hydrogen satisfies periodicity by being placed in group I, as well as in group VII.

In all groups except I, a distinct periodicity in the change of atomic weights (ratio of atomic weights) of elements of the main subgroups is found. In group I, the periodicity is broken only upon placing hydrogen in this group (hydrogen satisfies periodicity when placed in group VII).

The atomic volumes (ratio of atomic volumes) of the elements of the main subgroups, except for I and II, change periodically (for the zero group there is an insufficient number of results). In group I, periodicity is broken by placing hydrogen in this group, while radium causes the deviation for group II; by placing hydrogen into group VII, periodicity is satisfied.

Fig. 4 gives the change of the size of the crystalline positive ions of Pauling [6] in relation to the period number of the elements of the main subgroup. The radius of the ions in A is represented by the vertical axis, the period number, by the horizontal. In all groups with the exception of VII, a stepwise change of the radius occurs; a smooth curve is also found for group II upon transition from the second to the third period.

The heats of formation (ratio of the heats) of chlorides of the second, fourth and fifth periods show a periodic change; a smooth change occurs only in the third period. The heats of formation of halides of groups I, II, III and IV in the solid state (for group I in the gaseous state) also change periodically.

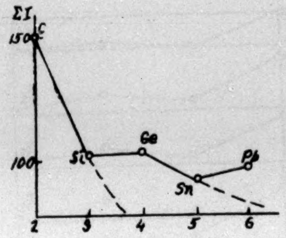

Fig. 5. Curve of the relation of the sum of the group potential to the atomic number of the elements of group IV.

The secondary periodicity in the change of properties of elements in a vertical direction on the main subgroup of the Mendeleev Table is related, evidently, to the relative decrease in the atomic size occurring with the occupation of the d and especially, f positions by electrons. Atomic size itself determines various properties of elements, and in particular, their ionization potentials. Thus, in group IV, the silicon atom is larger than the carbon atom, and correspondingly, has a smaller value for the ionization potential. If the structure of the germanium, tin and lead atoms was analogous to that of silicon and carbon, then the total group potential (i.e., $I_1 + I_2 + I_3 + I_4$) would have been on the dotted line (Fig. 5) which is an extension of the C - Si line. However, germanium because of the inclusion of the 10 d electrons, has a structure different from silicon, which results in a considerable contraction of the germanium atom, and the latter causes an increase in the ionization potential of germanium in comparison to that of silicon. Tin has a structure analogous to that of germanium (in it 10 electrons also occupy the d position) but tin is larger, and has a correspondingly smaller value for the ionization potential. If lead, the element following tin, had an analogous structure, then its ionization potential would have been on the dotted line constructed by continuing the Ge - Sn line. But lead has a different structure than tin (in it, in addition to the d position, 14 f positions are occupied by electrons) which results in a further relative contraction of the lead atom, and correspondingly, an increase of the ionization potential in comparison to that of tin.

The periodic change in the stability of oxygen compounds of the main subgroups of groups IV - VII in a vertical direction on the Mendeleev Table can be explained by the participation of a greater number of electrons in the formation of these compounds, equal to or close to the group number, and corresponding to a higher ionization potential number. Upon reaction of the elements with hydrogen, a periodic change in the vertical direction does not occur; this may be due to the fact that, during the formation of hydrogen compounds, the affinity of the elements for an electron (zero ionization potential), or a small number potential must be in effect, whereby the latter changes smoothly, or in either case, with less expression of periodicity.

SUMMARY

1. The relation between the tangents of the angle of inclination of lines expressing Moseley's Law, and the atomic number of elements is defined by a periodic curve with the following periods: H - He, Li - Ne, Na - Ni, Cu - Pd, Ag - Pt; the sixth period is begun by Au.

2. The ionization potentials of the elements of the main subgroups change periodically in the vertical direction on the Mendeleev Table in relation to the atomic number, wherein the periodicity is more expressed for potentials of higher order closest to the group number; the ionization potentials, the order of which exceeds the group number, change smoothly.

3. The periodic change, in the vertical direction, of the atomic number, atomic weight, atomic volume, and the radii of the crystalline positive ions for the main subgroups was shown.

4. The periodic change of the heats of formation of chemical compounds is related to the corresponding periodic change of the ionization potentials.

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THE MUTUAL SYSTEM OF LITHIUM AND COBALT SULFATES AND CHLORIDES

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The effect of cations of the eighth group on the character of ternary mutual systems is not given in the literature because of the absence of actual examples of ternary mutual systems with the above cations participating.

The ternary mutual system studied, $Li_2Cl_2 + CoSO_4 \rightleftarrows CoCl_2 + Li_2SO_4$, containing cations of elements of the marginal groups of the periodic table is of great interest for a more complete study of the effect of the position of elements in the periodic system on the character of ternary mutual systems.

The experimental section was conducted by the visual polythermic method with the aid of Yu. S. Butkova.

Binary systems. The binary systems $CoSO_4 - Li_2SO_4$ and $Li_2Cl_2 - Li_2SO_4$ were investigated by other authors and repeated by the authors of this communication. According to the data of Kalkanyi and Marotta [1], the system $CoSO_4 - Li_2SO_4$ had a eutectic containing 29%* of cobalt and melts at 595°. According to the author's data, the eutectic contains 27.5% of cobalt sulfate and melts at 590° (Table 1, Fig. 1).

The system $Li_2Cl_2 - Li_2SO_4$ was studied by M. Ya. Klochko [2]. According to his data, lithium chloride and sulfate form a eutectic containing 53.5% of lithium sulfate, melting at 478°. The polymorphic transformation of lithium sulfate corresponds to 572°. According to the authors' data, the eutectic contains 53% of lithium sulfate and melts at 478°. The polymorphic transformation temperature of lithium sulfate is 572°. A homeomorphic transformation is found at 564° on the fusion curve of lithium chloride (Table 2, Fig. 1).

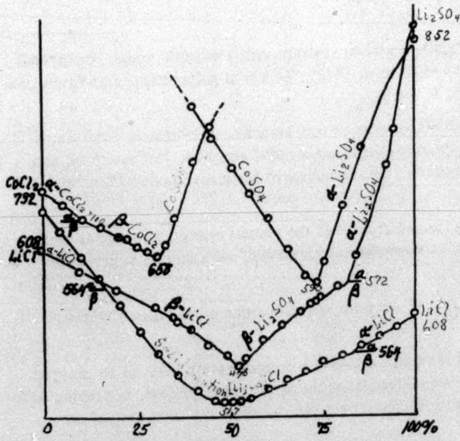

Fig. 1. Lateral sides of the squares of the mutual system.

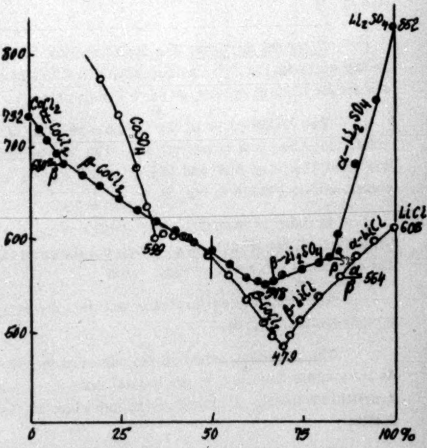

Fig. 2. Diagonal section.

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* All the percents are equimolecular.

TABLE 1

Expt. No.	Equimolecular per cent		Temp. of formation of first crystals
	$CoSO_4$	Li_2SO_4	
1	60	40	787
2	55	45	752
3	50	50	721
4	45	55	692
5	40	60	664
6	35	65	628
7	30	70	601
8	27.5	72.5	590
9	25	75	617
10	20	80	647
11	15	85	740
12	10	90	784
13	5	95	818
14	0	100	852

TABLE 2

Expt. No.	Equimolecular per cent		Temp. of formation of first crystals	Expt. No.	Equimolecular per cent		Temp. of formation of first crystals
	Li_2Cl_2	Li_2SO_4			Li_2Cl_2	Li_2SO_4	
1	100	0	605	12	40	60	508
2	90	10	582	13	35	65	525
3	80	20	562	14	30	70	540
4	70	30	544	15	27	73	550
5	65	35	532	16	26	74	552
6	64	36	528	17	25	75	556
7	60	40	518	18	20	80	567
8	55	45	503	19	15	85	600
9	50	50	491	20	7	93	700
10	47	53	478	21	5	95	740
11	45	55	489	22	0	100	852

TABLE 3.

Expt. No.	Equimolecular per cent		Temp. of formation of first crystals	Expt. No.	Equimolecular per cent		Temp. of formation of first crystals
	$CoCl_2$	$CoSO_4$			$CoCl_2$	$CoSO_4$	
1	100	0	732	8	72	28	663
2	95	5	713	9	70	30	658
3	90	10	700	10	68	32	673
4	85	15	690	11	65	35	700
5	80	20	680	12	60	40	760
6	78	22	676	13	55	45	800
7	75	25	672				

The system $Li_2Cl_2-CoCl_4$ was first studied by the authors. Lithium and cobalt chlorides form a continuous series of solid solutions with a minimum at 517° and 50% cobalt chloride. A homeomorphic transformation of lithium chloride is noted on the diagram at 565° (Table 4, Fig. 1)

Diagonal Sections. The stable section $CoCl_2-Li_2SO_4$ is a binary system with a eutectic which corresponds to the composition 65% lithium sulfate and 35% of cobalt chloride at 548°. At 575° a polymorphic transformation occurs for lithium sulfate, at 680°, cobalt chloride (Table 5, Fig.2).

The fusion curve of the unstable section $Li_2Cl_2-CoSO_4$ consists of four branches: α, β-lithium chloride, β-cobalt chloride, and cobalt sulfate. The intersection of the branches occurs at 564° and 14%, 479° and 31%, and 479° and 31%, and 599° and 65% of cobalt sulfate, respectively. The fusion curve has a maximum at 600° and 63% cobalt sulfate (Table 6, Fig. 2).

In order to investigate the surface of the initially formed crystals of the mutual system, 15 internal sections were studied, the directions of which are shown in Fig. 3. A short characterization of each section is given in the combined table and on Figs. 4 and 5.

The results of the experimental data are summarized in the form of a projection on the square of the mutual system (Fig. 6).

The transition points on the curves of the internal sections enabled the crystallization poles to be mapped. As is apparent from Fig. 6, the mutual system consists of seven crystallization poles: cobalt sulfate, occupying 30%; α, β-lithium sulfate, 17.1%; α, β-lithium chloride, 18.1%; α, β-cobalt chloride, 34.8% of the total area of the square.

The stable diagonal section cobalt chloride – lithium sulfate separates the square of the mutual system into two ternary systems: $CoCl_2-Li_2SO_4-Li_2Cl_2$ with a ternary eutectic E_1 of the composition: 44% lithium chloride, 36% lithium sulfate, 20% of cobalt chloride, melting at 452°, and $CoCl_2-Li_2SO_4-CoSO_4$ with a ternary eutectic

Combination Table

Section No.	Starting mixture of the components	M.p. of starting mixture	Component added	Branches of the crystallization curves and their intersections										Maxima on the curves		Fig. no.
				Branch I	Intersection of I and II		Branch II	Intersection of II and III		Branch III	Intersection of III and IV		Branch IV	%	t°	
					%	t°		%	t°		%	t°				
I	80% $CoCl_2$ + + 20% $CoSO_4$	679	Li_2SO_4	β-$CoCl_2$	63	530	β-Li_2SO_4	81	573	α-Li_2SO_4						4
II	45% Li_2SO_4 + + 55% $CoSO_4$	752	Li_2Cl_2	$CoSO_4$	17	510	β-Li_2SO_4 + + $\beta CoCl_2$	60	477	β-LiCl	85	564	α-LiCl	35	543	4
III	55% Li_2SO_4 + +45% $CoSO_4$	690	Li_2Cl_2	$CoSO_4$	13	530	β-Li_2SO_4									4
IV	65% Li_2SO_4 + + 35% $CoSO_4$	625	Li_2Cl_2	$CoSO_4$	7	551	β-Li_2SO_4	55	470	β-LiCl				27	562	4
V	70% Li_2SO_4 + + 30% Li_2Cl_2	540	$CoSO_4$	β-Li_2SO_4	46	507	$CoSO_4$							22	566	4
VI	50% Li_2SO_4 + + 50% Li_2Cl_2	494	$CoSO_4$	β-LiCl	2	475	β-Li_2SO_4	40	531	β-$CoCl_2$	52	549	$CoSO_4$	32	554	4
VII	30% Li_2SO_4 + + 70% Li_2Cl_2	546	$CoSO_4$	β-LiCl	21	452	β-$CoCl_2$	58	572	$CoSO_4$				55	574	4
VIII	25% Li_2SO_4 + + 75% Li_2Cl_2	557	$CoCl_2$	β-LiCl	43	490	α-$CoCl_2$									5
IX	5% Li_2SO_4 + 95% Li_2Cl_2	–	$CoCl_2$	β-LiCl	48	494	α-$CoCl_2$									5
X	75% Li_2Cl_2 + + 25% $CoCl_2$	562	$CoSO_4$	β-LiCl	21.5	484	β-$CoCl_2$	60	609	$CoSO_4$				55	615	5
XI	63% Li_2Cl_2 + + 37% $CoCl_2$	531	$CoSO_4$	β-LiCl	10	488	α-$CoCl_2$									5
XII	50% Li_2Cl_2 + +50 % $CoCl_2$	511	$CoSO_4$	α-$CoCl_2$	15	545	β-$CoCl_2$	55	621	$CoSO_4$				47	624	5
XIII	40% Li_2Cl_2 + + 60% $CoCl_2$	–	Li_2SO_4	β-$CoCl_2$	52.5	520	β-Li_2SO_4	80	575	α-Li_2SO_4						5
XIV	38% Li_2Cl_2 + + 62% $CoCl_2$	538	$CoSO_4$	α-$CoCl_2$	12	568	β-$CoCl_2$									5
XV	25% Li_2Cl_2 + + 75% $CoCl_2$	607	$CoSO_4$	α-$CoCl_2$	8	625	β-$CoCl_2$	43	643	$CoSO_4$				25	662	5

TABLE 4

Experiment No.	Equimolecular %		Temp. of formation of first crystals	Experiment No.	Equimolecular %		Temp. of formation of first crystals
	$CoCl_2$	Li_2Cl_2			$CoCl_2$	Li_2Cl_2	
1	100	0	732	13	47	53	519
2	95	5	707	14	45	55	522
3	90	10	680	15	40	60	530
4	85	15	656	16	35	65	539
5	80	20	628	17	30	70	548
6	75	25	600	18	25	75	557
7	70	30	572	19	20	80	565
8	65	35	549	20	15	85	575
9	60	40	532	21	10	90	585
10	55	45	521	22	5	95	595
11	52	48	518	23	0	100	608
12	50	50	517				

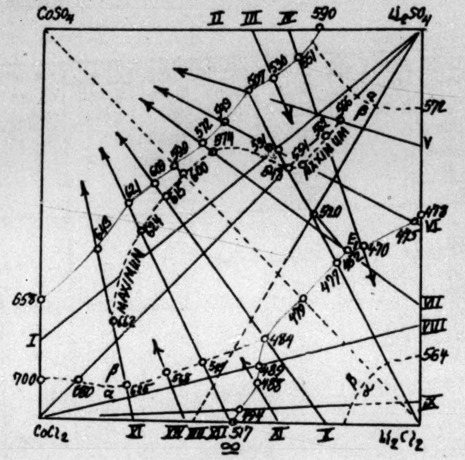
CoSO4
Li2SO4
CoCl2
Li2Cl2
II
III
IV
590
572
V
VI
VII
VIII
IX
X
XI
XII
XIII
XIV
I
658
700
564
478
517
∞
MAXIMUM
E1
E2
α
β
470
484
479
520

Fig. 3. Directions of the internal sections.

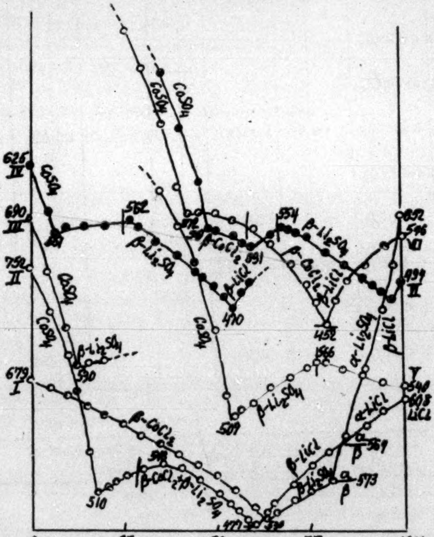

Fig. 4. Internal sections I − VII.

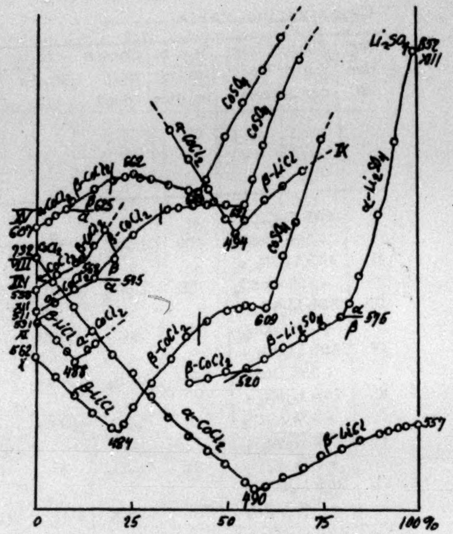

Fig. 5. Internal sections VIII − XV.

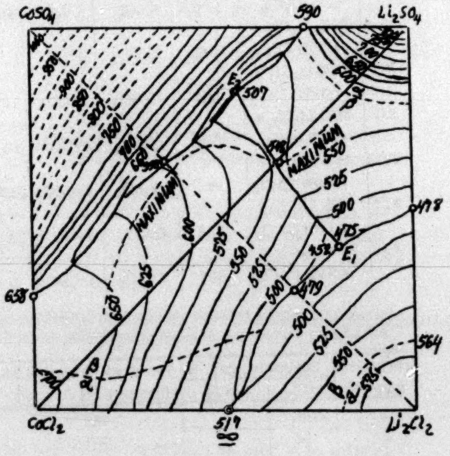
CoSO4
590
Li2SO4
CoCl2
517
∞
Li2Cl2
E2
507
MAXIMUM
550
525
500
478
475
E1
452
479
658
564
α
β
600
625
650
700
750
800

Fig. 6. Projection of the isotherms on the composition square.

TABLE 5

Experiment No.	Equimolecular %		Temp. of formation of first crystals
	$CoCl_2$	Li_2SO_4	
1	100	0	732
2	97	3	716
3	95	5	703
4	92	8	692
5	90	10	680
6	85	15	668
7	80	20	654
8	75	25	641
9	70	30	628
10	65	35	615
11	60	40	605
12	55	45	595
13	50	50	582
14	45	55	570
15	40	60	557
16	37	63	550
17	35	65	548
18	33	67	553
19	30	70	557
20	25	75	564
21	20	80	571
22	18	82	575
23	15	85	600
24	10	90	674
25	5	95	746
26	0	100	852

TABLE 6

Experiment No.	Equimolecular %		Temp. of formation of first crystals.
	Li_2Cl_2	$CoSO_4$	
1	100	0	608
2	95	5	593
3	90	10	577
4	85	15	562
5	80	20	533
6	75	25	508
7	72	28	494
8	70	30	481
9	67	33	494
10	65	35	503
11	60	40	530
12	55	45	556
13	50	50	581
14	45	55	594
15	43	57	597
16	40	60	599
17	37	63	600
18	35	65	599
19	33	67	628
20	30	70	672
21	25	75	730
22	20	80	770

E_2 of the composition: 30% lithium sulfate, 54% cobalt chloride, and 16% cobalt sulfate, melting at 507°. The continuous solid solutions with a minimum at 517° which are formed in the system of cobalt and lithium chlorides, are destroyed by the addition of a small amount of the third component.

In order to make the melting points and the positions of the invariant points, as well as the common crystallization curves of the components more accurate, projections of the above points and curves of the square on the sides $CoCl_2 - Li_2Cl_2$ and $Li_2Cl_2 - Li_2SO_4$ were made.

SUMMARY

1. The system of lithium and cobalt chlorides and sulfates was first studied by the visual-polythermic method of physico-chemical analysis, and was assigned to the irreversible-mutual systems by its thermochemical effect, as well as by its character. But the deviation of the ridge in the pole cobalt chloride and lithium sulfate from the plane of the stable diagonal section is an indication of some reversibility of the exchange reaction.

2. The reaction is directed toward the stable pairs: cobalt chloride-lithium sulfate, which agrees with the thermochemical effect of the exchange reaction, equal to 6.82 kcal per equivalent.

3. The stable diagonal section of cobalt chloride and lithium sulfate separates the ternary mutual system into two ternary systems: $CoCl_2 - Li_2SO_4 - Li_2Cl_2$ with the ternary eutectic at 452° and $CoCl_2 - Li_2SO_4 - CoSO_4$ also with a ternary eutectic point, at 507°.

4. The solid solution with a minimum at 517° and 50% lithium chloride, which is formed in the lateral binary system of cobalt and lithium chloride, is destroyed within the mutual system by the addition of small amounts of the other components.

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SUMMARY

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LITERATURE CITED

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[illegible] J. Am. Chem. [illegible]

STRUCTURE OF COBALTIC AND NICKEL HYDROXIDE PRECIPITATES

S. I. Sobol

Cobaltic hydroxide, $Co(OH)_3$ is usually prepared by the oxidation of a cobaltous chloride or sulfate solution in neutral or weakly acidic medium with strong oxidizing agents (hypochlorite, persulfate, electric current, etc.). The precipitate contains varying amounts of zeolytic water in relation to the conditions of preparation, which are removed by heating over 100°.

Different authors assign various structures to the precipitate. In earlier investigations [1], $Co(OH)_3$ was assigned a crystalline structure; however, LeBlank and Müller [2] could not detect a crystal lattice in the hydroxide Co_2O_3, precipitated from solution, by means of X-rays, while Co_2O_3 obtained by a dry method (fusion) shows it readily. For this reason [2], they considered that cobaltic hydroxide has a disordered spatial lattice and cannot be considered a crystalline substance. In order finally to solve this problem of the structure of cobaltic hydroxide precipitate, it was necessary to investigate it by many methods. The structure of the precipitate of $Co(OH)_3 \cdot xH_2O$ formed by hypochlorite from chloride and sulfate solutions having a pH 1.5 - 2.0 and at 20 to 80° were investigated.

The investigations were conducted in transmitted and polarized light at small magnifications, as well as with the aid of an electron microscope; electronograms were taken for a preparation deposited on a collodion film at magnifications up to 9000 times.

For visual investigations and photography in visual and polarized light, drops of freshly precipitated pulp were placed on a glass slide and covered with a cover glass.

All operations with such preparations were conducted within a short time, maximum 1-2 hours, and thus were protected from all sorts of distortions possibly arising during drying of the precipitate, as for example crystallization of salts from the mother liquor.

Investigation of cobaltic hydroxide precipitates in non-polarized light showed the following:

1. In mass, the particles of the residue obtained at the same rate of addition of hypochlorite from sulfate solutions, as well as from hot solutions, are considerably coarser than those obtained from chlorides, as well as from cold solutions (Figs.1 - 3).*

2. Particles of the residue always have an eneven form; the borders of the particles are sometimes folded.

3. Fine and medium particles are translucent and are colored yellow; the coarse are opaque and are colored only at the borders; in large mass (on the filter, or in the pulp) cobaltic hydroxide precipitates have a dark brown or sometimes a black color.

4. An examination of the precipitate removed from the pulp at the time of the precipitations of the cobalt with sodium hypochlorite at 80° from an acidified starting solution ($pH \approx 1.5$)showed that the color of the particles changes sharply when the pH of the medium became 2.3 - 2.5; even fine, translucent, yellow particles gradually lost translucency and became dark brown, almost black; upon chemical analysis, this residue showed that the cobalt in it was oxidized to more than trivalency.

5. Decrease of the rate of addition of hypochlorite to the solution, all other conditions being equal, led to the preparation of a coarser, on the average, precipitate. However, no amount of slowing down of the precipitation of cobaltic hydroxide could lead to the preparation of particles with a noticeable crystal lattice.

Upon examination of particles of the precipitate in transmitted polarized light, and upon rotation of the objective, the particles disappeared from the field of vision, a phenomenon characteristic for non-crystalline substances.

The electronograms of the finer particles of cobaltic hydroxide are shown in Figs. 4 - 9,* which were precipitated from a chloride solution at 80° and pH 1.5, and they very graphically show the absence of crystalline structure in the particles of the precipitate.

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* See plate, page 1115.

It is apparent from the photographs that the finest particles of the hydroxide, which have a cross section of tenths of a micron, were fused together to form aggregates of various coarseness. Therefore, coarse particles of $Co(OH)_3$ are formed by the coagulation of particles of colloidal size, i.e., particles of the cobaltic hydroxide visible to the eye or at slight magnifications with the visual microscope are gels, not crystals.

Because coarse particles are formed by the combination of a large number of very small ones having an irregular form, the coarse particles must be viewed as not being monolithic, but as friable aggregates. Electronic rays give only the shape of such aggregates (shown in Figs. 7 and 8*) because these figures do not show any monolithic structure in coarse particles.

During the process of combination of the particles, micro-volumes filled with mother liquor remain isolated from the surface within the coarse aggregates being formed; special experiments showed that substances present in the mother liquor, which are not coprecipitable with cobaltic hydroxide, are not removed from the particles of the precipitate even with thorough and continued repulping. However, these impurities are to a great extent (80-84%) removed from an initially repulped wet precipitate of cobaltic hydroxide by pressing the latter under a pressure of 80-100 kg/cm². These experiments served as important proof of the porosity of coarse cobaltic hydroxide particles and supplemented the information on the structure of the latter obtained by other methods of investigation.

Higher nickel hydroxidesobtained by various methods are not in a chemical sense, homogenous substances; most probably they are solid solutions of $Ni(OH)_4$ and $Ni(OH)_2$ of varying composition [3].

The structure of these precipitates was more than once the subject of an investigation. X-ray investigations [2] of the higher nickel hydroxides showed that they were so greatly dispersed that, after a 3-day drying at 100°, no trace of any crystal lattice could be seen on the X-raygrams.

The higher nickel hydroxides were investigated only with ordinary transmitted light at magnifications up to 160 times. The nickel precipitates were translucent, dark brown, flocculant particles of irregular form, disappearing from the field of view upon examination with polarized light and rotation of the objective. With increase in temperature, the coarseness of the particles increased (Figs. 10 and 11*); increase of the pH of the medium had the same effect. Fig. 12* shows the initial stage of formation of coarse aggregates by the combination of fine particles occurring during the precipitation with neutral sodium hypochlorite from a nickel sulfate having a pH 3.96 and at 80°.

Visual observation with a binocular microscope of samples of the pulp removed during the process of precipitation over short intervals of time, showed that the fine particles, formed initially, combined rapidly after the addition of sodium hypochlorite portion ended, and after 3-5 minutes, large friable aggregates were formed in the pulp (Fig. 13*)By changing the focus of the microscope, the many internal spaces in such primary aggregates could be seen. However, because of the great size of these aggregates, when one of these is found in focus, the other leaves it, and sometimes it appears to be monolithic.

After many minutes, sometimes hours, the primary friable aggregates have time to condense considerably; this process which is observed to proceed with time, is aided by a slight stirring of the pulp at higher temperatures. It is interesting that, in contrast to particles of nickel hydroxides, those of cobaltic hydroxide precipitated at low temperatures, do not grow as coarse upon further heating and mixing of the pulp. Fig. 13*shows such condensed aggregates.

It is interesting to point out that, in contrast to nickel precipitates, it was possible to observe and find separate stages in the growth of coarseness of cobaltic hydroxide particles only with the use of much higher magnifications; the particles of nickel hydroxide are themselves considerably coarser.

Therefore, it can be considered confirmed that particles of cobaltic hydroxide and higher nickel hydroxides do not have a noticeable crystalline lattice and must be viewed as gels.

Upon the precipitation of ferric hydroxide, a close analog of cobalt and nickel in the periodic system, in relation to the temperature conditions and rate of precipitation, residues in amorphous gel like state, as well as in clearly expressed crystalline form, can be obtained. In the case of the precipitation of trivalent cobalt and tetravalent nickel hydroxides, no sort of deceleration of precipitation results in the formation of an obviously crystalline precipitate. The reason for this must be sought in the various properties of Fe^{III}, Co^{III}, and Ni^{IV}. Fe^{III} is very stable in aqueous solution and in the presence of certain other ions, as for example the chloride ion. This is

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See Plate, page 1115.

the result of the small relative value of the redox potential of the pair $Fe^{III}-Fe^{II}$ (0.77 V). Co^{III} and, especially Ni^{IV}, in such solutions, and especially at higher temperatures, are very unstable, since according to the value of the redox potential ($Co^{III}-Co^{II}$ 1.82V, while for $Ni(OH)_4-Ni^{II}$ 2.0 V[3]), they can not only oxidize Cl' ion atomic chlorine, but the hydroxyl ion (with the evolution of oxygen), as a result of which the concentration of Co^{III} and Ni^{II},, within a short time (seconds and fraction of seconds), falls to an insignificant value approaching the equilibrium defined by the solubility product of the corresponding solid phase.

On the strength of this phenomenon, conditions for the hydrolysis of salts of Co^{III} and Ni^{IV} are radically different from those for the hydrolysis of Fe^{III} salts, namely, the necessary time and material is lacking for the formation of a crystal lattice of cobaltic hydroxide and the higher nickel hydroxides, and the primary particles of these hydroxides formed in very dilute (for Co^{III} and Ni^{IV}) solutions naturally cannot have coarse sizes. The formation of primary particles of the precipitate of $Co(OH)_3$ and $Ni(OH)_4$ can only occur at the time of the introduction of some strong oxidizing agent; after it is no longer available in the solution, almost at once the formation of primary particles of the precipitate stops. The gel like particles of the precipitate, possessing an enormous surface energy, tend to decrease the store of the latter by combining (coagulation) into coarse particles.

SUMMARY

1. Cobaltic and higher nickel hydroxide precipitates were subjected to microscopic investigation in transmitted and polarized light; in addition, the cobaltic hydroxide precipitates were investigated by means of the electron microscope.

2. It was found that coarse cobaltic and nickel hydroxide particles do not have a crystalline structure and are formed by coagulation of particles of colloidal size; therefore, these hydroxides are gels.

3. A suggestion was made as to the reasons why cobaltic and higher nickel hydroxides did not form a crystal lattice during the process of precipitation.

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PHYSICO-CHEMICAL CONDITIONS OF PRECIPITATION, HEAT OF FORMATION AND SOLUBILITY PRODUCT OF COBALT HYDROXIDE

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Cobaltic hydroxide is usually prepared by the oxidation of cobaltous salts in heated neutral or weakly acidic solution by some strong oxidizing agent, sodium, potassium, and calcium hypochlorite, gaseous chlorine, ozone, persulfate, or an electrical current [1, 2, 3, 4]. However, literature reports on the physico-chemical conditions and chemism of the precipitation of cobalt hydroxide are very scarce and contradictory, while the heat of formation and solubility product have only one result which must be viewed as an approximate one.

Certain authors [1, 2, 3, 4, 5, 6] describe the oxidation-precipitation of cobalt by hypochlorite in this form:

$$2CoSO_4 + NaClO + 5H_2O = 2Co(OH)_3 + NaCl + 2H_2SO_4; \quad (1)$$

$$2CoSO_4 + NaClO + 4NaOH + H_2O = 2Co(OH)_3 + 2Na_2SO_4 + NaCl; \quad (2)$$

$$2CoSO_4 + 3NaClO + NaCl + 3H_2O = 2Co(OH)_3 + 2Na_2SO_4 + 2Cl_2; \quad (3)$$

$$2CoSO_4 + 3NaClO + H_2O = Co_2O_3 + O + NaHSO_4 + NaCl + Cl_2. \quad (4)$$

combining in one equation, apart from the basic reaction, a series of parallel side reactions which proceed with the evolution of chlorine and oxygen.

These authors do not formulate a viewpoint on the question of the mechanism of the process of oxidation-precipitation of cobalt. Other authors [7,8] start from the assumption that the chemical oxidant was not strong enough to guarantee the oxidation of the $Co^{\cdot\cdot}$ to the $Co^{\cdot\cdot\cdot}$ in the solution as the first stage of the reaction (1) - (4), because the redox potential of the process $Co^{\cdot\cdot} \rightarrow Co^{\cdot\cdot\cdot}$ is very great. For this reason the second group of authors believe that the first stage must necessarily be the precipitation of the hydrated cobalt oxide, and the second, the oxidation of $Co(OH)_2$ by the hypochlorite, chlorine, or some other chemical oxidizer to $Co(OH)_3$.

Drexel, for example, gives the following order for the reaction for the case of the application of a neutral solution of hypochlorite:

$$2NaClO + 2H_2O \rightleftarrows 2NaOH + 2HClO; \quad (5)$$

$$CO^{\cdot\cdot} + 2OH^{\cdot} \rightleftarrows Co(OH)_2 \text{ solid}; \quad (6)$$

$$2Co(OH)_2 \text{ solid} + HClO + H_2O \rightleftarrows 2Co(OH)_3 \text{ solid} + HCl; \quad (7)$$

the excess hypochlorite, consisting of 50% for the above, is catalytically decomposed by the cobalt hydroxide.

$$NaClO \rightarrow NaCl + \tfrac{1}{2}O_2. \quad (8)$$

Bray [8] cites (7) for the case of the application of hypochlorite and reaction (9) for the gaseous chlorine.

$$2Co(OH)_2 \text{ solid} + 2NaOH + Cl_2 \text{ gas} = NaCl + Co_2O_3 \cdot 3H_2O. \quad (9)$$

Only the application of a very active oxidizing agent as an electrical current, is able, according to Drexel, to cause the oxidation of cobalt on the anode (as the first stage of the process), if the electrolysis is conducted in dilute sulfuric acid

$$2CoSO_4 + H_2SO_4 + 2e^- = Co_2(SO_4)_3 + 2H^{\cdot}; \quad (10)$$

the hydroxide appears in the second stage of the process as a result of the hydrolysis of the cobalt oxysulfate

$$Co_2(SO_4)_3 + 3H_2O \rightleftarrows Co_2O_3 + 3H_2SO_4. \quad (11)$$

Drexel recommends that the precipitation of cobaltic hydroxide be done at pH 2.5-2.8 with hypochlorite;

Chufarov and co-workers [9] found that at room temperature, cobaltic hydroxide is formed in solutions of chlorides by the action of hypochlorous acid at pH 3.0-3.2, in solutions of sulfates, at pH 4.4-6.0.

The authors' results indicate that hypochlorous acid and gaseous chlorine cause the precipitation of cobalt hydroxide from much more acidic solution having a pH which sometimes is less than unity. Here the formation of cobaltous hydroxide, as the first stage of the formation of cobaltic hydroxide, is absolutely excluded since it is known [10, 11] that the precipitation of $Co(OH)_2$ requires a considerably higher pH (of the order of 6-7).

The relative activity of the cobalt ions of different valency in the solution corresponding to activity of the oxidizing agent used, is determined by the Nernst equation

$$E = E_0^{Co^{\cdot\cdot}/Co^{\cdot\cdot\cdot}} + \frac{RT}{nF} \ln \frac{a_{Co^{\cdot\cdot\cdot}}}{a_{Co^{\cdot\cdot}}}, \qquad (12)$$

where the activity of $C^{\cdot\cdot\cdot}$ is independently related to the activity product of cobaltic hydroxide.

$$L_{aCo(OH)_3} = a_{Co^{\cdot\cdot\cdot}} \cdot a^3_{OH'}. \qquad (13)$$

If it is considered that the activity of OH' is defined by the ion product of water

$$K_W = a_{H^{\cdot}} \cdot a_{OH'}. \qquad (14)$$

and that, by definition, $-\log a_{H^{\cdot}} = pH$ (15), substituting the corresponding values into (12), and transposing to logarithms to the base ten, we obtain:

$$E = E_0^{Co^{\cdot\cdot}/Co^{\cdot\cdot\cdot}} + bT(\log L_a - 3 \log K_W - 3pH - \log a_{Co^{\cdot\cdot}}). \qquad (16)$$

Equation (16) expresses the relationship of the process of the oxidation of $Co^{\cdot\cdot} \rightarrow Co^{\cdot\cdot\cdot}$ and the subsequent hydrolysis of the $Co^{\cdot\cdot\cdot}$ salts, relating the important parameters, temperature, pH of the solution, activity of the bivalent cobalt ions, with the physico-chemical properties of the oxidizing agent (by means of the values of the true redox potential E).

Analysis of equation (16) shows that, if the representation of the consecutiveness of the separate stages of the process of preparation of cobaltic hydroxide (first the oxidation of $Co^{\cdot\cdot}$ into $Co^{\cdot\cdot\cdot}$, then the hydrolysis of the $Co^{\cdot\cdot\cdot}$ salts), which was the basis of its derivation, is correct, then, during the precipitation of the hydroxide at constant temperature, the following relationships must be found: based on the oxidation and precipitation of the cobalt in the form of cobaltic hydroxide, i.e. based on the decrease in the active concentration of the bivalent cobalt, the pH of the solution must gradually increase; the stronger the oxidizing agent used, i.e., the higher the value of the redox potential (E), the smaller will the equilibrium pH of the solution be at the given active concentration of cobaltous oxide.

Nothing can be said beforehand about the effect of the increase in temperature of the solution on the direction of the transposition of the curves of change of equilibrium pH during the oxidation-precipitation of cobalt; E can increase or decrease in relation to the properties of the oxidizing agent and with increase in temperature, which introduces some uncertainty into the relation between the constant (at the given temperature) coefficients of equation (16). This question can be answered experimentally in each particular case.

The heat of formation of cobaltic hydroxide had been measured by Thomson in 1882-1886. Thomson measured the heat of the reaction:

$$2CoCl_{2aq} = NaClO_{aq} = H_2O_{liquid} = 4NaOH_{aq} = 2Co(OH)_{3solid\ crystals} + 5NaCl \qquad (17)$$

in a calorimeter.

Britske and Kapustinsky [12] calculated the heat content of $Co(OH)_3$ at 18° to be equal to 177,000 cal/mole for formation from the elements) from his data.

Almost forty years after Thomson's investigation, it was shown during an investigation of (17) proceeding in neutral medium [6] that the thin surface layer of particles of the precipitate was oxidized to cobalt peroxide which very actively decomposed the hypochlorite catalytically, which then could enter into the main reaction. The amount of decomposed hypochlorite is almost undeterminable and depends on many small factors (rate of addition of the hypochlorite into the solution, efficiency of stirring of the pulp, etc.); for this reason it can be supposed that less than the corresponding stoichiometric amount of hypochlorite participated in reaction (17) in Thomson's experiments. On the other hand, the amount of alkali used was always sufficient for the complete precipitation of the cobalt in the form of cobaltous hydroxide $Co(OH)_2$, and for this reason, a certain (undeterminable) part of the latter must have been always unoxidized.

In view of the above data which, it must be thought, were unknown to Thomson, it must be recognized that the method chosen by him for the determination of the heat of formation of $Co(OH)_3$ was not applicable, and in principle, could not give correct results. However, no one, after Thomson, used other physico-chemical methods for the determination of ΔH.

It must also be mentioned that Thomson considered cobaltic hydroxide crystalline; later investigators showed that [13, 14] $Co(OH)_3 \cdot xH_2O$ does not have a noticeably expressed spatial lattice and is a gel.

The solubility product of cobaltic hydroxide was calculated at 25° by Latimer [15]; starting from the value of the heat of formation (−173,000 cal/mole) obtained by Thomson, and an approximate accepted entropy of formation of 103.2 cal/degree, Latimer obtained the free energy of formation of $Co(OH)_3$ from the elements, −142,000 cal/mole, from which $L = 2.5 \cdot 10^{-43}$. Because of the uncertainty of the results of Thomson's experiments, used by Latimer as the basis for the calculation of the solubility product, the value of the latter (according to Latimer) must only be accepted as a first approximation. Undoubtedly in any case, cobaltic hydroxide is a very poorly soluble compound.

The solubility of the hydroxide, equal to $5.6 \cdot 10^{-3}$ mg/liter or about 10^{-7} g-ions of $Co^{\cdots}$ per l., was found with the aid of the radioactive isomer of cobalt [16]. There was no possibility of examining the original paper [16] and the conditions under which this value was obtained (pH, temperature, and others) is not known.

Considering all of the above on the question of the determination of the heat of formation and solubility product of $Co(OH)_3$, it was necessary to once more determine these constants using a method which excluded the above errors.

For this reason, the equilibrium constant of the hydrolysis reaction of $Co^{\cdots}$ was determined (for several temperatures in the interval 19-81°)

$$Co^{\cdots} + 3OH' = Co(OH)_{3\,solid}, \tag{18}$$

from which

$$K' = \frac{1}{a_{Co^{\cdots}} \, a^3_{OH'}}, \tag{18'}$$

which is identical (in a thermodynamic sense) with the reaction

$$Co^{\cdots} + 3H_2O = Co(OH)_{3\,solid} + 3H^{\cdot}, \tag{19}$$

from which

$$K' = \frac{a^3_{H^{\cdot}}}{a_{Co^{\cdots}}}; \tag{19'}$$

reaction (19) more accurately describes the chemism of the hydrolysis of the salts of $Co^{\cdots}$ in an acidic medium.

From (19') we obtain

$$\log K' = -3pH - \log a_{Co^{\cdots}}, \tag{20}$$

which makes it possible to apply the known equation

$$\log \frac{K'_2}{K'_1} = -\frac{Q_1(T_2 - T_1)}{4.575\, T_1 T_2} \tag{21}$$

to find Q_1, the heat effect of the reaction of formation of $Co(OH)_3$ from the ions $Co^{\cdots}$ and OH', since the heats of formation of: $Co^{\cdot\cdot}$ from Co [12] equal to +16500 cal/g-ion., $Co^{\cdots}$ from $Co^{\cdot\cdot}$ [17], equal to + 33700 cal/g-ion, (thus the heat of formation of $Co^{\cdots}$ from elementary cobalt in solution is + 50200 cal/g-ion, and OH' from the elements [12], equal to 54660 cal/g-ion, is known from the literature, then there is no difficulty in calculating Q, the heat of formation of cobaltic hydroxide from the elements.

Using the values of $a_{Co^{\cdots}}$ and $a_{OH'}$ found experimentally, is also easy to determine the activity product of cobaltic hydroxide, L_a (13).

EXPERIMENTAL

The precipitation of cobaltic hydroxide was effected by sodium hypochlorite solution from solutions of $CoSO_4$ and $CoCl_2$. The solution in a flask was efficiently stirred, and the hypochlorite was added dropwise from a burette. The true redox potential generated in the solution was measured by means of the usual compensation scheme by smooth platinum electrode versus a saturated calomel one. The flask with solution was placed into an aqueous thermostat the temperature of which was held with an accuracy of ± 0.5°.

TABLE 1

Change in Parameters During the Precipitation of Cobaltic Hydroxide from a Chloride Solution

Experiment 98-k, pH of the starting solution 1.13; in the solution~40 g/liter of NaCl; hypochlorite: Active Cl, 122 g/liter; NaOH 19 g/liter.

Experiment 99-k, pH of the starting solution, 1.16; in the solution,~40 g/liter of NaCl, hypochlorite: Active Cl, 122 g/liter, NaOH 19 g/liter.

Temperature	Composition of the solution (g/liter)			E (in V)		Logarithm of the activities		log L_a	log K'
	Co··	Cl'	pH	During the addition of the hypochlorite	During the determination of pH	Co··	Co···		
19.0°	44.8	84.6	2.21	1.308	1.288	−0.430	− 9.605	−44.775	+ 2.970
	37.7	79.0	2.14	−	1.338	−0.517	− 9.832	−44.432	+ 2.417
	28.3	75.3	2.25	1.358	1.318	−0.655	− 8.650	−43.900	+ 2.900
	22.0	75.3	2.35	1.368	1.318	−0.762	− 9.472	−44.442	+ 2.422
	11.2	63.4	2.50	1.358	1.288	−1.036	−10.216	−44.716	+ 2.716
	5.2	53.0	2.78	1.353	1.264	−1.328	−10.918	−44.218	+ 2.578
	2.58	−	2.83	1.328	1.252	−1.553	−11.348	−44.848	+ 2.858
	0.70	−	3.20	1.312	1.248	−1.958	−11.828	−44.228	+ 2.228
						Average		−44.49	+ 2.709
81.0	39.8	67.5	1.48	1.308	1.229	−0.484	−10.469	−43.869	+ 6.024
	33.1	63.6	1.52	1.328	1.238	−0.578	−10.428	−43.668	+ 5.902
	24.4	60.0	1.53	1.308	1.248	−0.718	−10.433	−43.643	+ 5.843
	20.9	56.0	1.58	1.328	1.238	−0.785	−10.635	−43.695	+ 5.295
	15.8	54.8	1.61	1.321	1.228	−0.900	−10.900	−43.870	+ 6.070
	10.62	−	1.83	1.326	1.241	−1.056	−10.866	−43.176	+ 5.376
	8.50	49.2	1.86	1.318	1.224	−1.143	−11.191	−43.411	+ 5.611
	7.64	51.9	1.80	1.308	1.247	−1.180	−10.915	−43.315	+ 5.415
	5.83	54.5	1.73	1.310	1.256	−1.300	−10.870	−43.385	+ 5.680
	4.56	40.2	1.91	−	1.242	−1.377	−11.177	−43.247	+ 5.447
	2.74	−	1.95	−	1.248	−1.538	−11.253	−43.203	+ 5.403
						Average		− 43.50	+ 5.65

The accuracy of the potential measurement was ±0.002 V. In order to measure the pH of the solution (by means of a potentiometer with glass electrodes), a sample was removed from the pulp after the addition of the determined quantity of hypochlorite. The accuracy of the pH measurement was not lower than ±0.05. After the determination of the pH, the sample was filtered, and the concentration of the cobalt and chloride ions determined.

The cobalt solutions were prepared from cobalt sulfate and chloride of Pure for Analysis grade; the solutions were initially purified from iron hydroxide, with cobaltous hydroxide and filtered; the filtrate was acidified with C.P. sulfuric or hydrochloric acid, respectively, to a pH of about 1.2. The sodium hypochlorite solutions were prepared by passing purified chlorine gas into a solution of C.P. sodium hydroxide at temperatures not greater than 15°.

The actual potential was measured at once after the addition of the hypochlorite and the measurements were then continued periodically until E stopped changing. A sample of the pulp was then removed, and the pH of the solution measured.

TABLE 2

Changes in Parameters During Precipitation of Cobaltic Hydroxide from Sulfate-Chloride Solutions. Experiments 95-k, 96-k, 97-k; starting solution of cobalt sulfate without the addition of NaCl; the removal of the sample was conducted at 19.2° after 4 hours, 50.5°, after 1-2 hours, and at 81°, 1.5 hours.

Temperature	Composition of the solution g/liter			E(in V)		Logarithm of the activity		log L_a	log K'
	$Co^{\cdot\cdot}$	Cl'	pH	During the addition of the hypochlorite	During the determination of pH	$Co^{\cdot\cdot}$	$Co^{\cdot\cdot\cdot}$		
19.2°	18.1	9.47	2.40	1.398	1.358	−0.844	−8.821	−43.621	+ 1.621
	11.8	13.85	2.43	1.393	1.358	−1.018	−8.993	−43.693	+ 1.693
	7.25	17.70	2.63	–	1.339	−1.208	−9.508	−43.608	+ 1.608
	5.83	18.50	2.68	–	1.333	−1.276	−9.676	−43.636	+ 1.636
						Average		−43.64	+ 1.642
50.5	20.5	7.53	1.69	1.408	1.328	−0.793	−9.268	−44.098	+ 4.198
	14.5	9.47	1.95	1.398	1.298	−0.932	−9.877	−43.927	+ 4.027
	7.86	12.6	1.76	1.398	1.338	−1.174	−9.489	−44.109	+ 4.209
	3.47	13.8	1.93	1.388	1.337	−1.468	−9.803	−43.883	+ 4.020
						Average		−44.01	+ 4.113
81.0	25.2	6.10	1.40	1.361	1.211	−0.706	−10.966	−44.596	+ 6.756
	20.5	11.25	1.46	1.361	1.262	−0.790	−10.340	−43.750	+ 5.915
	17.3	18.40	1.38	1.351	1.278	−0.864	−10.180	−43.840	+ 8.024
	8.3	20.30	1.45	1.351	1.254	−1.149	−10.809	−44.259	+ 6.414
	2.74	–	1.70	1.361	1.224	−1.553	−11.643	−44.346	+ 6.003
	0.72	–	2.01	1.351	1.228	−1.958	−12.008	−43.778	+ 5.933
	0.095	–	3.30	1.351	1.232	−2.796	−12.766	(−40.646)*	(+ 2.846)*
						Average		−44.15	+ 6.232

TABLE 3

Change in the Parameters During Precipitation of Cobaltic Hydroxide from Sulfate Solutions. Experiment 92-k; starting solution of $CoSO_4$ with 40 g/liter of Co; pH 1.06; temperature 80°; hypochlorite: active Cl, 96 g/liter; NaOH, 30 g/liter.

Composition of the solution (g/liter)			E (in V)		Logarithm of the activity		log L_a	log K'
$Co^{\cdot\cdot}$	Cl'	pH	During the addition of the hypochlorite	During the determination of pH	$Co^{\cdot\cdot}$	$Co^{\cdot\cdot\cdot}$		
35.2	(1.3)	1.13	1.437	1.413	−0.547	−7.897	−42.307	+ 4.507
33.6	(2.0)	1.25	1.413	1.402	−0.556	−8.066	−42.116	+ 4.316
32.6	(3.5)	1.28	1.412	1.400	−0.585	−8.135	−42.095	+ 4.295
29.4	5.0	1.32	1.406	1.391	−0.635	−8.310	−41.150	+ 4.350
27.6	6.50	1.36	1.396	1.385	−0.663	−8.418	−42.133	+ 4.333
24.8	(8.0)	1.38	1.392	1.370	−0.704	−8.674	−42.334	+ 4.734
22.0	9.42	1.40	1.385	1.366	−0.762	−8.797	−42.397	+ 4.597
19.9	(10.5)	1.52	1.376	1.355	−0.804	−8.984	−42.224	+ 4.424
18.9	11.57	1.48	1.378	1.357	−0.827	−9.037	−42.397	+ 4.597

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* The reason for the extreme deviation from the average values obtained with large concentrations of $Co^{\cdot\cdot}$ in the solution is the start of the peroxidation of cobaltic precipitate at pH>2.5 at the above temperatures [14].

TABLE 3 — (continued)

Composition of the solution (g/liter)			E (in V)		Logarithm of the activity			
Co··	Cl'	pH	During the addition of the hypochlorite	During the determination of pH	Co··	Co···	log L_a	log K'
16.3	(12.6)	1.50	1.373	1.354	−0.886	−9.041	−42.341	+4.541
14.7	13.77	1.47	1.363	1.346	−0.924	−9.239	−42.629	+4.829
11.1	(14.7)	1.55	1.361	1.332	−1.036	−9.551	−42.701	+4.901
9.65	(15.74)	1.60	1.361	1.335	−1.092	−9.567	−42.567	+4.767
8.40	(16.8)	1.60	1.361	1.339	−1.149	−9.564	−42.564	+4.764
7.35	17.97	1.52	1.361	1.333	−1.194	−9.694	−42.934	+5.134
						Average. .	−42.39	+4.61

Notes: 1) Samples were taken after 5-10 minutes; 2) figures in parentheses are interpolated values (the same in Tables 4 and 5).

TABLE 4

Change in Parameters During Precipitation of Cobaltic Hydroxide from Chloride Solutions.

Experiment 90-k; starting solution of $CoCl_2$, with 50 g/liter of Co··; temperature 81°; hypochlorite, Cl_{active} 74 g/liter; NaOH 24 g/liter. Experiment 93-k; starting solution of $CoCl_2$ and $NiCl_2$ containing 30 g/liter of Co and 60 g/liter of Ni, pH 1.42; temperature 80°; hypochlorite: Cl_{active} 101.4 g/liter; NaOH, 41.6 g/liter

Composition of the solution (g/liter)			E (in V)		Logarithm of the activity			
Co··/Cl'	Cl···	pH	During the addition of the hypochlorite	During the determination of pH	Co··	Co···	log L_a	log K'
40.3	72.4	1.83	1.306	1.273	−0.491	− 9.88	−42.190	+ 4.390
34.5	63.4	1.73	1.316	1.298	−0.650	− 9.59	−42.300	+ 4.500
27.7	63.4	1.80	1.306	1.303	−0.664	− 9.614	−42.014	+ 4.214
22.5	−	1.82	1.320	1.306	−0.754	− 9.664	−42.004	+ 4.204
18.3	63.4	1.88	1.320	1.303	−0.838	− 9.80	−41.960	+ 4.160
14.7	−	1.85	1.318	1.302	−0.924	− 9.89	−42.140	+ 4.340
11.2	54.3	1.96	1.322	1.311	−1.036	− 9.89	−41.810	+ 4.010
9.10	−	1.95	1.326	1.305	−1.114	−10.04	−41.990	+ 4.190
5.25	60.4	1.93	1.324	1.311	−1.319	−10.17	−42.180	+ 4.380
3.65	−	1.98	1.326	1.314	−1.456	−10.26	−42.120	+ 4.320
1.04	−	2.07	1.328	1.324	−1.842	−10.50	−42.090	+ 4.290
0.66	−	2.30	1.296	1.269	−1.958	−11.39	−42.290	+ 4.490
						Average	−42.00	+ 4.29
25.8	101.4	1.50	1.333	1.316	−0.695	− 9.445	−42.745	+ 4.945
22.4	(104)	1.56	1.320	1.314	−0.757	− 9.527	−42.647	+ 4.847
19.5	107.7	1.57	1.322	1.311	−0.812	− 9.632	−42.722	+ 4.922
15.9	(97)	1.70	1.325	1.321	−0.896	− 9.561	−42.261	+ 4.461
14.8	86.9	1.58	1.333	1.326	−0.921	− 9.531	−42.591	+ 4.791
13.6	(85.4)	1.70	1.331	1.317	−0.955	− 9.685	−42.385	+ 4.585
12.1	84.0	1.78	1.328	1.315	−1.000	− 9.755	−42.215	+ 4.415
10.9	83.2	1.77	1.326	1.311	−1.046	− 9.866	−42.356	+ 4.556
10.1	82.5	1.85	1.334	1.310	−1.076	− 9.898	−42.148	+ 4.348
						Average	−42.45	+ 4.65

Notes. In both experiments, the samples were removed after ten minutes.

A state close to equilibrium was usually established at room temperature after 1.5 - 2 hours, and at higher temperatures (50 - 80°), after 30-60 minutes.

In order to judge the state of the process under conditions approximating the industrial, in a series of experiments, the removal of the samples and the basic measurements (E and pH) were conducted 5 - 10 minutes after the addition of each portion of the hypochlorite. The results of the experiments are given in Tables 1-5.

The activity coefficients of $CoSO_4$ and $CoCl_2$ were taken from data [15, 18]. The calculation of L_a and K'_1 for temperatures above room temperature, required a knowledge of the value of the normal potential of Co·· → Co··· and the ion product of water. $E_0^{Co··/Co···}$ at 20° was taken as being equal to 1.82 V, and the temperature coefficient, 0.00168 V per degree [4, 17]; $E_0^{Co··/Co···}$ for 50° was obtained as 1.87 V and 1.93 V for 80 ± 1° by extrapolation. The value of the ion product of water for various temperatures was taken from [19].

The activity of the Co··· was calculated with equation (12), the logarithmic hydrolysis constant of Co··· by equation (20), and the activity product $L_{a\,Co(OH)_3}$ from equation (13).

All the values calculated on the basis of experimental data are given in the same Tables (1-5).

TABLE 5

Change in the Parameters During Precipitation of Cobaltic Hydroxide from Sulfate Solutions Experiment 94-k; starting solution $CoSO_4$; pH 1.06; Hypochlorite Cl_{active} 90.4 g/liter; NaOH 32 g/liter; temperature, 80°. The samples were removed after 5-10 minutes.

Composition of the solution (g/liter)			E (in V)		Logarithm of the activity			
Co··	Cl'	pH	During the addition of the hypochlorite	During the determination of pH	Co··	Co···	log L_a	log K'
33.8	(2.1)	1.15	*	1.344	−0.568	− 8.898	−42.248	+ 5.448
31.5	4.35	1.26		1.350	−0.600	− 8.850	−42.870	+ 5.070
29.1	−	1.28		1.334	−0.638	− 9.018	−43.158	+ 5.178
24.4	24.3	1.40		1.335	−0.719	− 9.199	−42.799	+ 4.999
22.0	(25)	1.40		1.326	−0.762	− 9.312	−42.912	+ 5.112
20.5	25.4	1.43		1.318	−0.790	− 9.500	−43.010	+ 5.210
18.6	(26)	1.45		1.319	−0.832	− 9.532	−42.982	+ 5.182
14.5	30.0	1.46		1.299	−0.932	− 9.932	−43.352	+ 5.552
12.1	34.0	1.52		1.284	−1.005	−10.205	−43.445	+ 5.645
11.3	(36)	1.53		1.300	−1.032	−10.002	−43.212	+ 5.412
8.8	37.6	1.63		1.294	−1.125	−10.185	−43.095	+ 5.295
7.90	(42.0)	1.66		1.301	−1.168	−10.118	−42.938	+ 5.138
3.87	(53)	1.71		1.305	−1.432	−10.332	−43.002	+ 5.202
2.86	53.6	1.78		1.288	−1.538	−10.688	−43.148	+ 5.348
2.12	(54)	1.82		1.288	−1.620	−10.800	−43.140	+ 5.340
1.01	55.8	2.00		1.294	−1.854	−10.904	−43.704	+ 4.904
						Average	− 42.98	+ 5.31

Because in these experiments sodium hypochlorite was used as the oxidizing agent, and a certain amount of gaseous chlorine is evolved from the solution in the process of oxidizing cobalt, then the following processes participate in the generation of the compromise (actual) potential in the solution:

$$2Cl' = Cl_2 + 2e^-, \qquad E_0 = 1.36\ V, \qquad (22)$$

$$Cl' + H_2O = HClO + H^{\cdot} + 2e^-, \qquad E_0 = 1.50\ V, \qquad (23)$$

$$Cl_2 + 2H_2O = 2HClO + 2H^{\cdot} + 2e^- \qquad E_0 = 1.64\ V. \qquad (24)$$

The corresponding equations for the actual redox potential of each of these reactions are as follows:

$$E = E_0^{Cl'/Cl_2} - \frac{RT}{nF} \ln \frac{a^2_{Cl'}}{a_{Cl_2}} \qquad (22')$$

$$E = E_0^{Cl'/HClO} - \frac{RT}{nF} \ln \frac{a_{Cl'}}{a_{HClO} a_{H^{\cdot}}}, \qquad (23')$$

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* No measurements made.

$$E = E_0^{Cl_2/HClO} - \frac{RT}{nF} \ln \frac{a_{Cl_2}}{a^2_{HClO} \cdot a^2_{H}} \,. \qquad (24')$$

In order to make possible an examination of the effect of the various factors determining the E and pH during the precipitation of the cobalt [16], the measurement of E and pH was conducted in dilute solutions of sulfuric acid during titration with hypochlorite solution. The results of the experiments are shown on Figs. 1 and 2.

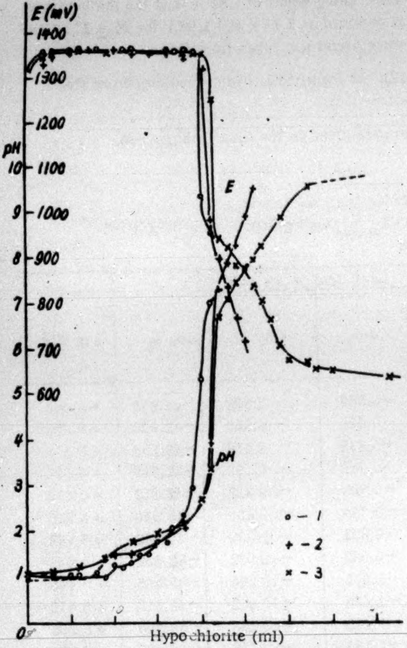

Fig. 1. Effect of the temperature on the change in E and pH during titration of 1/5 N H_2SO_4 (with the addition of 40 g/liter of NaCl) with an alkaline solution of sodium hypochlorite.
1) At 24°; 2) at 50°; 3) at 80°.

As it was expected from equations (22'), (23'), (24'), the actual redox potential of the solution at pH below 3 (i.e., in the pH region of the precipitation of cobaltic hydroxide at 19-81°), decreased with the increase of the concentration of Cl' in solution, and as the experiment showed, did not vary with the pH and the temperature of the solution.

Returning to Tables 1-5, it is apparent that E* and its tendency to change with the time of the oxidation-precipitation of cobalt with hypochlorite indicates that hypochlorous acid, not containing cobalt, is found in the solution: the greater the concentration of the chloride ion in the cobalt solutions, the lower is E at the time of the precipitation of the cobalt, the weaker, therefore, the oxidizing ability of the hypochlorite in such solutions.

Fig. 3 shows that, in accordance with equation (16), the decrease of the oxidizing strength of the agent used leads to a shift of the curves of the equilibrium values of the pH during the precipitation of cobalt in the region of higher pH values, while Figs. 3, 4, and 5 confirm the completely obvious relation between the pH and the concentration of the bivalent cobalt during the oxidation of the latter to the trivalent, and the formation, in equilibrium with a solution, of the precipitate of $Co(OH)_3$. It is apparent on these same figures, that, with increase in temperature of the pulp, the curve of the equilibrium value of pH is sharply shifted into the region of more acidic solutions.

It is apparent from Tables 1-5 that the values of log K' and log L_a show a small variation from the average during the extending of the precipitation time, and that the corresponding values for removal of samples after 5-10 minutes and after 1-1.5 hours after the addition of the hypochlorite are also very similar. All of this indicates that the system of solution–precipitate for cobaltic hydroxide approaches a state close to the equilibrium within a very short time.

It is also apparent from these results that the activity coefficient $L_{a\,Co(OH)_3}$ increases with the temperature (Table 1); a considerable sorption of the sulfate ion by the precipitate occurs in the sulfate solutions which somewhat distorts the picture of the change of L_a during the increase in temperature (Table 2); Thus the weight ratio of $Co^{\cdots}$: SO_4'' in precipitates obtained at about 80°, varied from 1:0.1 to 1:0.2, while at lower temperatures, the sorption of the SO_4'' was still higher.

For this reason, the most reliable of all of the thermodynamic values were given by experiments in chloride solutions because the side processes (sorption of the anion) were at a minimum.

Considering the above, the following values (according to Table 1) can be accepted for the activity product of $Co(OH)_3$ for temperatures: 19° $L_a^{19°} = 3.2 \cdot 10^{-45}$, 81° $L_a^{81} = 3.2 \cdot 10^{-44}$.

Increase of the equilibrium constant (K') of the hydrolysis reaction of $Co^{\cdot\cdot}$ with the increase of the

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* The actual potential was always recalculated versus the hydrogen electrode.

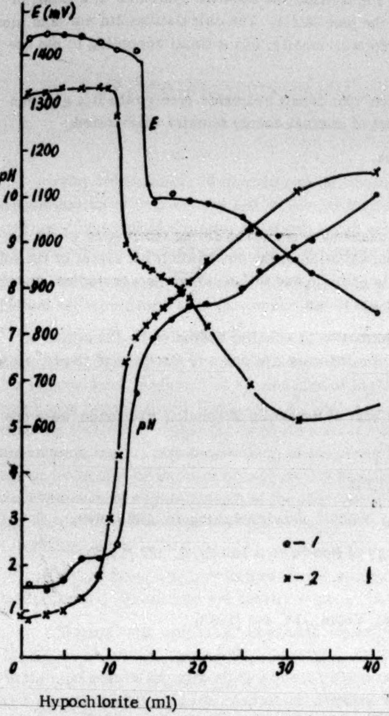

Fig. 2. Effect of the concentration of the chloride ion on the change of E and pH during titration of a 1/10 N H_2SO_4 with an alkaline solution of sodium hypochlorite. 1) Without NaCl in the starting solution; 2) with 200g/liter of NaCl.

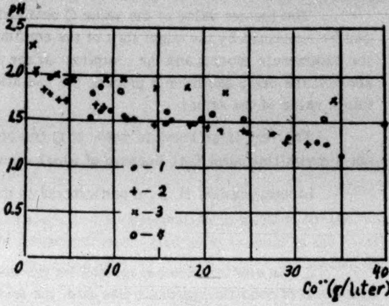

Fig. 3. The effect of the presence of the chloride ion in cobalt solutions on the change of the position of the equilibrium pH curve of the solution during the precipitation of cobaltic hydroxide with sodium hypochlorite.
1-2 Sulfate solutions; 3-4 chloride solutions.

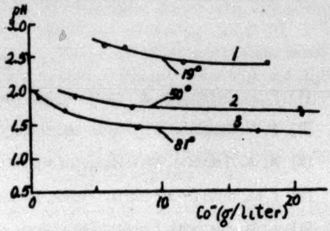

Fig. 4. Effect of temperature and concentration of Co˙˙ on the equilibrium pH value of the solution during the precipitation of cobaltic hydroxide.
1) Experiment No. 95, at 19°, 2) experiment No. 96, at 50°; 3) experiment No. 97, at 81°.

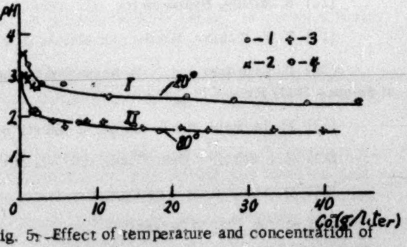

Fig. 5. Effect of temperature and concentration of Co˙˙ on the equilibrium pH value of the solution during the precipitation of cobaltic hydroxide with sodium hypochlorite.
1) Experiment No. 98-k; 2) experiment No. 100-k; 3) experiment No. 90-k; 4) experiment No. 101-k.
I - at 20°; II - at 80°.

temperature indicates the endothermic character of the reaction.

The following value is obtained for the reaction in chloride solutions using the data in Table 1.

$$Q_1 = -22500 \text{ cal.},$$

while from the data of other pairs of experiments (100-k and 101-k), the results of which are not given in consideration of economy of space, the following values were obtained for the value of Q_1: for the temperature interval 19.0-50.2°, 33,900 cal; 50.2-81.0°, 36,300 cal; 19.0-81.0°, 35,000 cal. Therefore, the heat effect of the formation of $Co(OH)_3$ from the elements has the following value (in the interval 19-81°): for precipitation from chloride solutions, +236,980 cal/mole, for precipitation from sulfate solutions, +249,180 cal/mole.

The greater value of the value Q obtained for the precipitation cobaltic hydroxide from sulfate solutions can be explained by the slight shift of the equilibrium between the solution and cobaltic hydroxide as a result of the exothermic process and the sorption of the sulfate ion by the precipitate. The calculations did not take into account the other exothermic process, the hydration of the precipitate; usually, this is small according to the absolute value of the effect.

The very large absolute value of Q is supplementary proof that cobalt hydroxide precipitate is a gel, and not a crystalline solid [14], because of which a considerable store of internal energy remains unliberated.

Laboratician N. N. Ilyin participated in the investigation.

SUMMARY

1. An electrochemical method for the investigation of phenomena occurring during the process of the precipitation of cobaltic hydroxide was used, the relationships of the variation of the equilibrium pH values of the solution with temperature and concentration of the bivalent cobalt in chloride and sulfate solutions was studied, and the effect of the value of the redox potential of the oxidizing agent was shown.

2. The results obtained favor the representation of the formation of cobaltic hydroxide by the action of strong oxidizing agents as the oxidation of $Co^{\cdot\cdot}$ to $Co^{\cdot\cdot\cdot}$, and the subsequent hydrolysis of the dalts of the trivalent cobalt.

3. More accurate values of the activity product and the heat of formation of cobaltic hydroxide were obtained.

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PHYSICO-CHEMICAL ANALYSIS OF SYSTEMS WITH INDIUM SULFATE

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The development of experiments on the study of the processes of complex formation in solution for the determination of composition and molecular state of the complex compounds stimulated great interest in the investigation of systems of the type A-B-solvent with various methods of physico-chemical analysis, which resulted in the development of new methods for the investigation of such systems [1].

In the present communication basic results are reported of the physico-chemical investigation of systems of indium sulfate-sulfuric acid (or ammonium sulfate) in aqueous solutions.

Indium sulfate is comparatively readily soluble in water. From neutral solutions, this salt crystallizes with nine, and according to more recent results [2], with ten molecules of water, $In_2(SO_4)_3 \cdot 10H_2O$. From solutions containing sulfuric acid, a product of the addition of $In_2(SO_4)_3$ with sulfuric acid precipitates, which is regarded in the literature as the complex acid $HIn(SO_4)_2 \cdot 3^1/_2H_2O$ analogous to the crystallo-hydrate of the same type of compound of thallium $HTl(SO_4)_2 \cdot 4H_2O$ [3], or as the acid salt $InH(SO_4)_2$ [4]. Indium sulfate forms double salts with a series of monovalent metals (and ammonium) of the general type $MeIn(SO_4)_2 \cdot 12H_2O$ and $MeIn(SO_4)_2 \cdot 4H_2O$ [5]. The number of molecules of water of crystallization to a great degree depends on the nature of the monovalent metal and the conditions of crystallization of the salts. For example, the following salts of this type were obtained: $K_2SO_4 \cdot In_2(SO_4)_3 \cdot 8H_2O$, $Na_2SO_4 \cdot In_2(SO_4)_3 \cdot 8H_2O$ [5], $Rb_2SO_4 \cdot In_2(SO_4)_3 \cdot 24H_2O$, $Cs_2SO_4 \cdot In_2(SO_4)_3 \cdot 24H_2O$ [6], $(NH_4)_2SO_4 \cdot In_2(SO_4)_3 \cdot 24H_2O$ [7].

All of these salts are formed by the mixing of concentrated solutions of these components taken in equimolecular ratios. These salts are readily soluble. Hydrolysis occurs upon boiling the solutions [5, 6].

Double salts with alkyl substituted ammonium cations are also known, as for example: $(CH_3NH_3)_2SO_4 \cdot In_2(SO_4)_3 \cdot 4H_2O$, $2(C_2H_5NH_3)_2SO_4 \cdot In_2(SO_4)_3 \cdot 7H_2O$, $3(p\text{-}C_5H_{11}NH_3)_2SO_4 \cdot In_2(SO_4)_3 \cdot 6H_2O$ and several others [8]. These salts possess great stability to heat. Their melting points are over 300°. In a series of cases, these salts also possess optical activity. Analogous complex halide salts of substituted ammonium bases (in contrast to the sulfates) crystallize without water, for example: $2(C_2H_5)_4NCl \cdot InCl_3$, $2(CH_3)_4NBr \cdot InBr_3$, and others [8].

All of the above mentioned double salts of indium sulfate were studied mainly for preparative purposes, to develop a method for the preparation of these salts out of solution certain physico-chemical properties such as: melting point, solubility, etc., were also investigated.

Solutions of these salts had scarcely been investigated in the physico-chemical sense. This remark is also true for systems of indium sulfate-sulfuric acid-water.

Ensslin [2], studying the system InC_3-SO_3-H_2O by method of solubility and densities, established that the following sulfates are formed in this system at temperatures between 20 and 60°: $In_2(SO_4)_3 \cdot nH_2O$ ($n = 10, 6, 5, 4$); $In_2(SO_4)_3 \cdot H_2SO_4 \cdot 7H_2O$; $2In(OH) \cdot (SO_4) \cdot 5H_2O$.

The decahydrate, $In_2(SO_4)_3 \cdot 10H_2O$ is a white readily soluble salt. According to Ensslin, it is formed in solutions containing from 10 to 20 weight % of free sulfuric acid. Solutions containing less than 3% of the acid result in the formation of basic salts. At a concentration of sulfuric acid greater than 30%, a salt of the composition $In_2(SO_4)_3 \cdot H_2SO_4 \cdot 7H_2O$ is formed, which precipitates in the form of shiny white tablets or plates. Crystallization occurs at room temperature.

The anhydrous salt of indium sulfate is obtained by heating $In_2(SO_4)_3 \cdot H_2SO_4 \cdot 7H_2O$ to 250°.

EXPERIMENTAL

The problems of the present investigation were to study the possibility of using electroconductivity (and cryoscopy) as a method of phyisco-chemical analysis of systems of the type A-B-solvents, to establish whether or

TABLE 1

The Specific Electroconductivity of the System $In_2(SO_4)_3-H_2SO_4-H_2O$;

0.1 molar solution

Mole % $In_2(SO_4)_3H_2SO_4$	Specific electroconductivity x · 10^3 (found) at t°				Specific electroconductivity x · 10^3 (calculated)* at t°			
	0	20	30	40	0	20	30	40
0	31.28	42.30	45.61	49.46	31.28	42.30	45.61	49.46
20	25.23	34.40	37.42	40.30	26.68	36.30	39.37	42.76
40	20.32	27.55	29.78	32.19	22.08	30.37	38.14	36.22
50	18.02	24.42	26.57	28.53	19.78	27.39	30.03	33.85
60	15.83	21.44	23.68	25.46	17.49	24.40	26.91	29.60
100	8.29	12.48	14.46	16.36	8.29	12.48	14.46	16.36

TABLE 2

Specific Electroconductivity of the System $In_2(SO_4)_3-(NH_4)_2SO_4-H_2O$;

0.1 M molar solution.

Mole % $In_2(SO_4)_3/(NH_4)_2SO_4$	Specific electroconductivity x · 10^3 at t°					
	Measured			Calculated		
	20	30	40	20	30	40
0	16.60	19.87	23.30	16.60	19.87	23.30
10	15.70	18.81	22.02	16.17	19.33	22.61
20	15.15	–	21.00	15.78	–	21.91
30	14.45	17.06	19.73	15.36	18.25	21.01
40	13.98	16.35	18.80	14.95	17.71	20.52
50	13.46	15.74	18.04	14.54	17.16	19.83
60	13.26	15.45	17.62	14.13	16.62	19.14
70	12.94	15.15	17.16	13.72	16.08	18.44
80	12.73	14.84	16.84	13.22	15.54	17.74
100	12.48	14.46	16.36	12.48	14.46	16.36

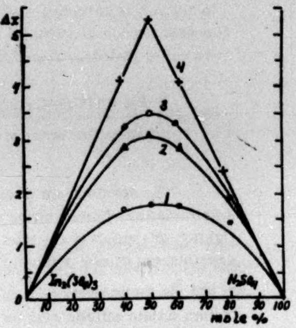

Fig. 1. Deviation of the specific electroconductivity of the system $In_2(SO_4)_3-H_2SO_4-H_2O$ 1) 0°; 2) 20°; 3) 30° and 4) 40° and a total concentration of 0.1 molar.

not complex compounds are formed in this type of system, to determine the composition of these complex compounds directly in solution, and to study the effect of temperature and concentration of the solution upon the isothermal electroconductivity curves. The experimental results of the investigation of the systems $In_2(SO_4)_3-H_2SO_4-H_2O$ and $In_2(SO_4)_3-(NH_4)_2SO_4-H_2O$ by the method of electroconductivity and cryoscopy are given below.

Anhydrous indium sulfate, $In_2(SO_4)_3$, was obtained by the heating of its salt $In_2(SO_4)_3 \cdot H_2SO_4 \cdot 7H_2O$ which was obtained by the solution of chemically pure In_2O_3 in an excess of sulfuric acid, according to Ensslin's data [2]. The solution obtained was evaporated on the water bath until the formation of the salt which was filtered on a porcelain funnel.

Then the salt $In_2(SO_4)_3 \cdot H_2SO_4 \cdot 7H_2O$ in the porcelain dish was dehydrated in a muffle furnace by raising the temperature gradually to 230-250° until the complete removal of SO_3 vapors, and then was kept at this temperature for some time. With such a method for the dehydration of the salt and the removal of sulfuric acid (complexly bound), a cloud of vapors of SO_3 is created over the dish of the indium sulfate in the muffle furnace, which prevents the formation of basic salts during the dehydration.

The anhydrous salt, $In_2(SO_4)_3$ obtained in this manner, had the form of a white powder. Analytical results: In –44.00%, SO_4 –56.05%; calculated for $In_2(SO_4)_3$; In –44.33%, SO_4 –55.67%.

The rest of the preparations were C. P., or correspondingly purified.

The measurement of the electroconductivity, and the graphic representation of the results were effected according to Ostromyslensky's and Dzhob's method.

The application of electroconductivity as a method of physico-chemical analysis according to Ostromyslensky-Dzhob was first used by I. A. Sheka and A. L. Goldinov for the investigation of the system $(NH_4)_2SO_4-MnSO_4-H_2O$ [9]; then this method was used and developed in other investigations of the Institute of General and Inorganic Chemistry of the Academy of Sciences of the Ukr. SSR. The usual technique for the measurement of the electroconductivity was used (with a vacuum tube signal generator). The temperature was kept within the limits of variation of ± 0.05° by means of a thermostat.

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* The calculation of the additive electroconductivity was made according to the rule of combination.

1. Table 1 gives the results of the measurement of the specific conductivity of the system $In_2(SO_4)_2$–H_2SO_4–H_2O at temperatures of 0,20, 30 and 40° and a total concentration of 0.1 molal Fig. 1 gives the deviation of the specific electroconductivity from additivity.

Fig. 2 gives the specific electroconductivity and deviation from additivity of the system $In_2(SO_4)_3$–H_2SO_4–H_2O at 40° and a total concentration of 0.05 molal

The magnitude of the deviation of the specific electroconductivity from additivity (Δx) was found by the subtraction of the found values of the specific electroconductivity from the calculated.

From the results in Table 1 and Figs. 1 and 2, it is found that the specific electroconductivity of the system $In_2(SO_4)_3$–H_2SO_4–H_2O increases with the increase of the total concentration (0.05-0.1 molar) of the system. The deviation from additivity, the maximum of which corresponds to equimolecular ratio of $In_2(SO_4)_3$ and H_2SO_4 for a 0.1 molar solution, has a greater value than for 0.05 molar solutions. At temperatures from 0-40°, the deviation from additivity increases with the temperature and the total concentration of the solution. On the basis of the above electroconductivity measurements, it can be concluded that a compound of the composition: $In_2(SO_4)_3 \cdot H_2SO_4$ exists in the solution at the temperatures and concentrations investigated. A cryoscopic investigation of the system $In_2(SO_4)_3$–H_2SO_4–H_2O was conducted by a method reported in a paper by Ya. A. Fialkov and I. D. Muzyka [10].

To 5 ml of an 0.1 molar solution of sulfuric acid were added increasingly greater, by weight, samples of $In_2(SO_4)_3$, and each time the depression was measured; the depression of the initial solution of sulfuric acid was arbitrarily taken as zero.

The results of the measurements are given on Fig. 3.

As is apparent from Fig. 3, there is an inflection on the change of depression curve in the region of an equimolecular ratio of $In_2(SO_4)_3$ and H_2SO_4. Later the path of the curve is determined by a linear relationship with the concentration of indium sulfate. The results of the cryoscopic measurement confirmed, therefore, the previously drawn conclusion, on the basis of the measurement of the electroconductivity, of the formation of the compound $In_2(SO_4)_3 \cdot H_2SO_4$, in the solution.

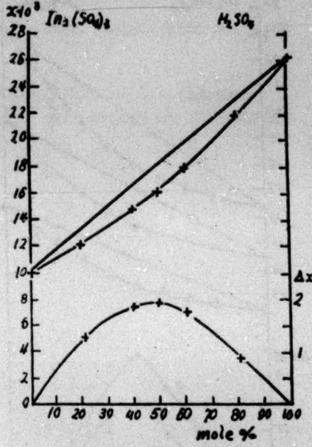

Fig. 2. Specific conductivity and deviation from additivity of the system $In_2(SO_4)_2$–H_2SO_4–H_2O at 40° and a total concentration of 0.05 molar.

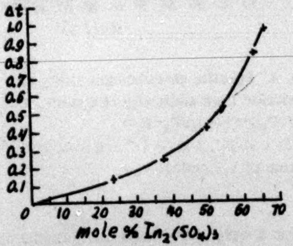

Fig. 3. Cryoscopy of the system $In_2(SO_4)_3$–H_2SO_4–H_2O.

2. The system $In_2(SO_4)_3$–$(NH_4)_2SO_4$–H_2O. A physico-chemical analysis of this sytem was made by the method of electroconductivity in the temperature interval of 20-40°.

The results of the investigation are given in Table 2 and Fig. 4.

The results in Table 2 and Fig. 4 indicate that a compound of the equimolar composition $In_2(SO_4)_3 \cdot (NH_4)_2SO_4$ exists in the system indium sulfate-ammonium sulfate-water (as in the solid phase); where, as in the system $In_2(SO_4)_3$–H_2SO_4–H_2O, the value of the deviation from additivity increases with the temperature.

For the solution of the problem of the structure of the complex compound $In_2(SO_4)_3 \cdot H_2SO_4$ and the nature of the ions in the solution, experiments were set up on the transport of ions in solutions of $In_2(SO_4)_3$ (1), as well as $In_2(SO_4)_3 \cdot H_2SO_4$ (2).

0.5 molar solutions were investigated. The electrolyzer consisted of three sections, the cathodic, the anodic, and the intermediate. Platinum electrodes were used. The feed bath was a direct current from the panel of a storage

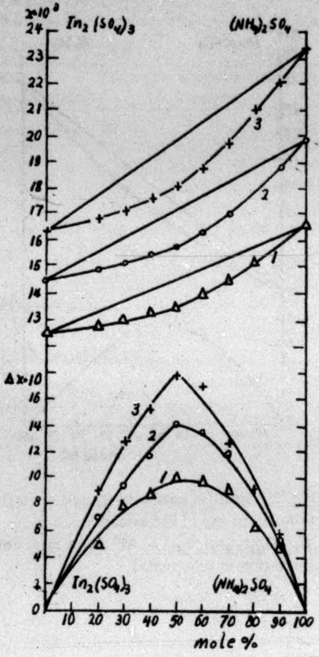

Fig. 4. Specific electroconductivity and deviation from additivity of system $In_2(SO_4)_3$–$(NH_4)_2SO_4$–H_2O. 1) 20°; 2) 30°, and 3) 40° and total concentration of 0.1 molarity.

battery. Current strength 16-30 mA. Duration of the experiments, 3-24 hours. The quantitative determination of indium was effected gravimetrically (as In_2O_3).

It was established that the transport number of indium to the cathode, upon going from electrolyte 1 to electrolyte 2, decreases by more than 2 times, from 0.16 to 0.06. In order to explain these facts it can be supposed that solutions of indium sulfate have a complex structure; complex ions are present in these solutions in which, evidently, indium also enters into the composition of the anions.

The introduction of sulfuric acid into the system $In_2(SO_4)_3$ – H_2O favors the stabilization of these complex anions, and shifts the equilibrium in the direction of their formation, because of which, the transport number of indium to the cathode decreases sharply almost to zero.

Therefore, there is a basis for proposing that the complex anion of the composition $In(SO_4)_2$ is formed in the system $In_2(SO_4)_3$–H_2SO_4–H_2O.

In conclusion, the author wishes to express profound gratitude to Prof. Ya. A. Fialkov for many valuable suggestions during this investigation.

SUMMARY

1. A physico-chemical analysis of the system $In_2(SO_4)_3$–H_2SO_4– H_2O was effected by the method of electroconductivity and cryscopy, and the system $In_2(SO_4)_3$–$(NH_4)_2SO_4$–H_2O, by the method of electroconductivity.

2. It was shown that a maximum value for deviation from additivity is found on the electroconductivity isotherm, which corresponds to an equimolar ratio of the components.

The deviation of the electroconductivity from the additive value in these systems increases with the temperature, (in the temperature interval studied) as well as with the concentration of the starting solutions.

3. By conducting, in this manner, an investigation within a wide temperature interval, the optimum temperature conditions for the formation and existence of complex compounds in solution could be established.

4. On the basis of the investigation conducted, it is possible to conclude that a compound $In_2(SO_4)_3 \cdot H_2SO_4$ existed in solution in the system indium sulfate-sulfuric acid-water, and $(NH_4)_2SO_4 \cdot In_2(SO_4)_3$ in the system indium sulfate, ammonium sulfate-water, solvated, apparently, by a determined amount of water molecules.

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CRYOSCOPY OF THE SYSTEM ALUMINUM CHLORIDE—ACETAMIDE—NITROBENZENE

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Aluminum halides possess the property to form a complex compounds with almost all classes of organic and inorganic compounds. Complex compounds of aluminum halides and acetamide are not reported in the literature. Meanwhile it seemed of interest to study the role of acetamide as an addend in complex formation reactions.

The character of bond of acetamide with the complex former remains unknown. A. Werner [1] considers that the bond is possible because of oxygen in the carbonyl group. B. N. Menshutkin [2], investigating acetamide complexes of magnesium bromide and iodide [3], considered that the relative stability of acetamide complexes was favored by the presence of the amido group. I. I. Chernyaev and L. A. Nazarov [5] showed that acetamide formed compounds of the inner complex type with salts of bivalent platinum salts with a valence bond resulting from the hydrogen of the amide group.

Physico-chemical investigations of systems containing acetamide and nitrobenzene were conducted by M. S. Ashkinazi [6], as well as by Ya. A. Fialkov and I. D. Muzyka [7] who showed that acetamide in nitrobenzene forms a compound $CH_3CONH_2 \cdot Br_2$ with bromine [6], and $CH_3CONH_2 \cdot ICl$ with iodine chloride [7].

The ternary system aluminum chloride—acetamide—nitrobenzene was studied by the method of cryoscopy. As V. V. Udovenko [8] and Ya. A. Fialkov and I. D. Muzyka [9] showed, cryoscopy is an effective method for the physico-chemical analysis of liquid systems.

EXPERIMENTAL

Commercial anhydrous aluminum chloride was sublimed and was stored in sealed test tubes. Nitrobenzene was allowed to stand for several days with a small amount of bromine, washed with sodium carbonate solution and water, dried over fused calcium chloride, and distilled. The fraction boiling over a one degree range was collected in the receiving tube which was rapidly sealed. The acetamide was recrystallized from alcohol, dried at 50-60°, and was stored in sealed test tubes.

The freezing point was determined in a Beckmann apparatus equipped with a magnetic stirrer. Two series of experiments were conducted, with concentrations of aluminum chloride in nitrobenzene of 0.1 to 0.216 moles of $AlCl_3$ per 1000 g of nitrobenzene. Because of the hygroscopicity of the solutions, the addition of acetamide was done each time with new portions of a nitrobenzene solution of aluminum chloride. Acetamide is not readily soluble in nitrobenzene but in solutions of aluminum chloride, the solubility of acetamide increases in proportion to the concentration of aluminum chloride in the solution. The concentration of acetamide was increased up to a molar ratio of $CH_3CONH_2 : AlCl_3 = 1.2 : 1$.

The results of the measurements are given in Tables 1 and 2.

TABLE 1

0.1 Moles of $AlCl_3$ per 1000 g of Nitrobenzene (1.31%)

$\frac{CH_3CONH_2}{AlCl_3}$ (in moles)	Freezing point according to Beckmann	Δt from that of nitrobenzene	$\frac{CH_3CONH_2}{AlCl_3}$ (in moles)	Freezing point according to Beckmann	Δt from that of nitrobenzene
Nitrobenzene	3.935°	0°	0.808	3.368°	0.567°
0	3.404	0.531	0.902	3.415	0.520
0.194	3.400	0.535	0.938	3.415	0.520
0.400	3.409	0.526	1.000	3.457	0.478
0.501	3.394	0.541	1.151	3.508	0.427
0.624	3.380	0.555	1.203	3.519	0.416

TABLE 2

0.216 Moles of $AlCl_3$ per 1000 g of Nitrobenzene (2.8 %)

$\frac{CH_3CONH_2}{AlCl_3}$ (in moles)	Freezing point according to Beckman	Δt from that of nitrobenzene	Δt calculated
Nitrobenzene	3.023°	0°	0°
0	1.617	1.406	1.406
0.204	1.615	1.408	1.652
0.402	1.555	1.468	1.893
0.500	1.557	1.466	2.011
0.599	1.542	1.481	2.128
0.800	1.539	1.484	2.374
0.899	1.631	1.392	2.493
1.002	1.660	1.363	2.616
1.118	1.772	1.251	2.756

These results are shown graphically on the Figure. The concentration of acetamide (in moles) per mole of $AlCl_3$ is laid off on the abscissas, and the depression in temperature, on the ordinates. The depression of solutions of acetamide in nitrobenzene were also determined. The results of the measurements are given in Table 3.

The molar depression in the freezing point K was calculated by the formula

$K = \frac{\Delta t}{n}$, where n is the molarity of the solution. The cryoscopic constant of nitrobenzene is 6.9° [10]. Therefore, acetamide is somewhat associated in nitrobenzene, and the degree of association $\alpha = \frac{6.9}{5.6} = 1.2$.

DISCUSSION OF RESULTS

As it is apparent from the Figure, the depression increases very insignificantly at first with the addition of acetamide to the nitrobenzene solution of aluminum chloride, and upon acquiring a concentration of acetamide equal to 0.8 moles per mole of $AlCl_3$, the depression decreases.

The insignificant rise in the depression in the region of small concentrations of acetamide, which is more noticeable for more concentrated solutions of aluminum chloride, is apparently due to the hydrolysis of the solution, which could not be avoided in spite of the precautions taken.

The depression was calculated assuming that a reaction did not occur between the aluminum chloride and acetamide. The results of the calculations are given in Table 2 column 4 ($\Delta t_{calc.}$). From these results, it follows that the increase in the depression caused by the acetone in the solution with a concentration of 0.2 moles of acetamide per mole of $AlCl_3$ must be 0.246°; actually it was 0.002°, which is found with the limits of experimental error.

TABLE 3

The Depression of Solutions of Acetamide in Nitrobenzene

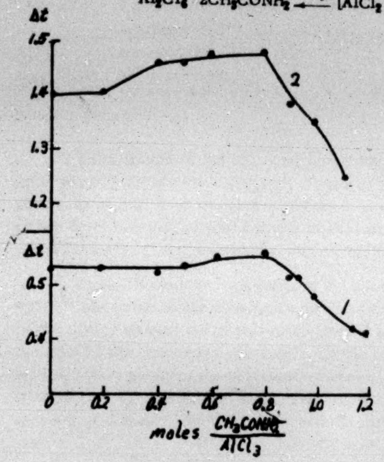
Nitrobenzene (in g)	Acetamide (in g)	Molality of the solution	Δt	Molar depression in freezing point
65.286	0.319	0.083	0.446°	5.4°
39.004	0.124	0.054	0.316	5.8
			Average	5.6

For solutions with a concentration of acetamide of 0.8 moles per mole of $AlCl_3$, the calculated increase in the depression is 0.968°, actually it was 0.078°. Therefore, the depression of the solutions up to a concentration of acetamide equal to 0.8, can be considered practically constant. The acetamide added to the solution of aluminum chloride combines chemically, which is also shown by the increase of the solubility of acetamide in nitrobenzene solutions of aluminum chloride.

At molar concentrations of acetamide of 0.8 moles per mole of $AlCl_3$, the depression starts to decrease. The path of the curve, of the relation between Δt – composition shows that aluminum chloride forms a complex with acetamide of the composition 1:1. According to B. I. Menshutkin's [11] data, aluminum chloride forms two compounds with nitrobenzene: $AlCl_3 \cdot 2C_6H_5NO_2$ and $AlCl_3 \cdot C_6H_5NO_2$. The shift of the maximum on the Δt-composition curve is related with the state of equilibrium between nitrobenzene and acetamide complexes of aluminum chloride, and possibly, with the formation of a ternary complex containing nitrobenzene and acetamide. The decrease in depression is due to the association of the acetamide complex, and apparently, to the simultaneous occurrence of the decrease of the electrolytic dissociation of the complex. The calculated molecular weight of the acetamide complex with nitrobenzene for 0.1-0.2 molal solutions has an average value of 244. According to the formula $AlCl_3 \cdot CH_3CONH_2$ it is 192. The degree of association is 1.27.

According to the views of N. N. Lebedev [12], complex compounds of aluminum chloride with organic substances exists in the form of ion pairs which shows a double molecular weight in concentrated solution. In dilute solutions, the dimer dissociates into ions according to the scheme:

$$Al_2Cl_6 \cdot 2CH_3CONH_2 \rightleftharpoons [AlCl_2 \cdot 2CH_3CONH_2]^+ + [AlCl_4]^-.$$



Cryoscopy of the System $AlCl_3-CH_3CONH_2-C_6H_5NO_2$.
1) 0.1 moles of $AlCl_3$; 2) 0.216 moles of $AlCl_3$.

The association of the complex must, therefore, be related to the degree of electrolytic dissociation. This can be confirmed by the study of the electroconductivity of the system.

SUMMARY

1. The depression in freezing point of 0.1 and 0.2 molal solutions of aluminum chloride in nitrobenzene-acetamide at a concentration of 0 to 1.2 moles of acetamide per mole of $AlCl_3$ was investigated. The Δt-concentration of acetamide diagram was constructed from these results.

2. The depression remains practically constant up to a concentration of the acetamide of 0.8 mole per mole of $AlCl_3$ during the addition of acetamide to a nitrobenzene solution of aluminum chloride, then the depression decreases.

3. The decrease of the depression is caused by the association of the complex of composition 1:1 formed in the solution. The molecular weight of the acetamide complex is 244. The degree of association is 1.27.

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* See Consultants Bureau Translation, page 1975.

CRYSTALLIZATION OF THREE-COMPONENT SYSTEMS WITH IMMISCIBLE LIQUID PHASES

F. S. Menshchikov

The question of the character of the distribution of the conoids in the region of immiscibility is of principal importance from the point of view of showing the distribution of the components into the conjugate liquid phases, as well as from the general theory of crystallization of monotectics. The material available in the literature on the determination of compositions of two conjugate liquid phases over wide intervals is extremely small, and is related mainly, to ternary systems with disruption in the solubility of one of the binary systems.

D. N. Tarasenkov, in a series of publications [1], first paid attention to the character of the form of the conoids and came to the conclusion that, in ternary systems having a disruption of solubility of the components only in one binary system, the continuation lines of all conoids intersect at one point lying on the continuation of one of the sides of the concentration triangle. In the case of such systems where there is a single region of immiscibility for two binary systems, the continuation lines of all conoids intersect at one of the apexes of the concentration triangle (Fig. 1). Up to now, D. N. Tarasenkov's conclusions have not been discussed in the literature even though they are of probable practical and theoretical interest.

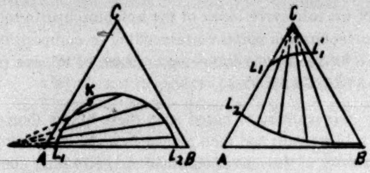


Fig. 1. Scheme for the distribution of conoids in the region of immiscibility according to D. N. Tarasenkov's hypothesis. k) Critical point of immiscibility; L_1 and L_2) first and second liquid layers.

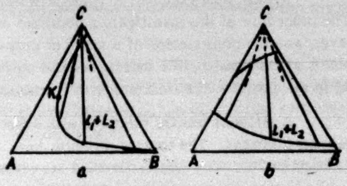


Fig. 2. Method of determining irregularity of the conoids k) Critical point of immiscibility; L_1 and L_2, first and second layers.

The author of this communication does not share D. N. Tarasenkov's view. It is clearly apparent from the material given in his papers that the abscissa of the intersection points of the continuation lines of the conoids have various values. Although the author correctly recognizes that there were large experimental errors for the calculation of the abscissa of the intersection of the continuation lines of the conoids, the experimental material given by him does allow that the conclusion made be considered completely proved In addition, D. N. Tarasenkov's conclusions place defined limits on certain systems during crystallization. These limits are not explained by any theoretical principles and are opposed to the experimental material obtained by the authors.

The binary homogenous system in which the immiscibility does not occur, was called by R. V. Mertslin the prevailing [2], since the reaction of components of the system frequently determines the character of the phenomena occurring in the given ternary system (Systems A-B, Fig. 2a). The second homogenous system in which the critical point is shifted onto separate isotherms, is called the supplementary (Systems A-C, Fig. 2a).

The character of the distribution of the conoids in the region of immiscibility is always such that they form clusters of straight lines radiating like a fan in the direction of the prevalent system. If, from the apex of the concentration triangle signifying the third component (not entering into the binary prevalent system), a series of rays are constructed going up to the region of immiscibility, then, generally speaking, the conoids can be found in various positions relative to these rays. Some conoids will diverge to the right of these rays, others to the left. Because of this, conoids of the right direction and those of the left are differentiated. If the conoids coincide accurately with the direction of the rays, then the direction is zero (Fig. 2b).

R. V. Mertslin proposed that "in the presence of a single region of immiscibility the direction of the conoids will also be single formed, and at the same time, if the subprevailing system occupies the right side of the composition triangle, then the direction of the conoids will be left, as well as the converse of the above" [2]. It must be mentioned that Mertslin's rule for systems in which immiscibility arises in two binary systems almost completely does not agree with Tarasenkov's rule, and therefore does not include those limitations in the behavior of systems during crystallization, which was previously discussed above.

The author's investigation had the following aims 1) to determine which of the two rules are correct for conoids of a two phase liquid state in ternary systems; 2) to determine whether R. V. Mertslin's or D. N. Tarasenkov's rule applies to limited conoids, i.e., to the isothermal lines of the primary crystallization from a two phase liquid state.

A solution of this problem will make it possible to go into a theoretical examination of the behavior of certain systems during crystallization. For this investigation, such systems were chosen in which reactions between the components did not lead to the formation of chemical compounds and solid solutions. Only three systems were studied: epichlorohydrin-toluene-water, phenol-naphthalene-water, and phenol-water-benzoic acid. A single region of immiscibility common for the two binary systems existed. The method of sectioning was used for the investigation of the distribution of conoids. The refractive index of one of the liquids and the crystallization point of one of the components were used as the properties to measure.

The substances used for these systems had the following characteristics: pure benzoic acid with m.p. 121.8°; phenol, redistilled at 181-181.5° and having an m.p. 41.8°; naphthalene, twice purified by sublimation, with m.p. 80.1°. Pure preparations of epichlorohydrin and toluene were not subjected to further purification.

System Epichlorohydrin-Toluene-Water. An Abbe refractometer was used for the investigation of this system. The procedure of the investigation consisted of the measurement of the refractive index of the epichlorohydrin-toluene layer, and the construction of a series of conodes passing through concentration points corresponding to composition points of equal refractive index. For this purpose, 4 sections, characterized by the following amounts of toluene (in %) in the initial binary mixture with epichlorohydrin were chosen: 87.28, 55.33, 31.80, 6.94.

A series of ternary mixtures with differing amounts of water was synthesized based upon these binary (homogenous) mixtures. The ternary mixtures were thoroughly shaken for 15 minutes and then placed in a thermostat for 24 hours at 25°. The results obtained are given in Fig. 3. The character of the curves obtained showed rather conclusively that the above rule of D. N. Tarasenkov was untrue. Actually, if the conoid continuations intersected at an apex of the concentration triangle (in this case at the apex corresponding to water – Fig. 4), then a gradual increase in the total concentration of water in the ternary system should not be reflected in the quantitative ratio of the components in the conjugate liquid phases, and the refractive index must remain unchanged. The observed change in refractive index indicated that the conoids do not have a zero direction; for this reason any of the sections

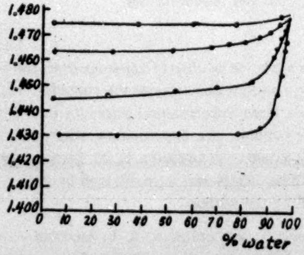


Fig. 3. Change in refractive index of the epichlorohydrin-toluene liquid phase in relation to the concentration of water in the ternary mixture.

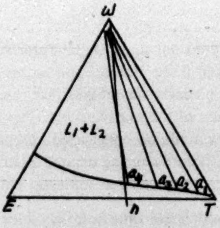


Fig. 4. Schematic diagram of the system epichlorohydrin-toluene-water showing the character of the change in composition of one of the liquid phases in the section W-n.

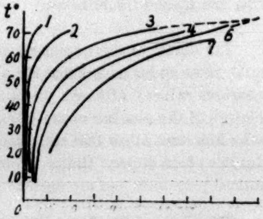


Fig. 5. Curve of the temperatures of beginning of formation of naphthalene crystals.

chosen intersect a series of conoids. In order to determine the character of the distribution of conoids the chosen sections were placed on the concentration triangle, and the concentration corresponding to equal refractive index values were found on these lines. A series of straight lines coinciding with the conoid directions were found by connecting the concentration points. In all, five of such lines were constructed conoids corresponding to the following refractive indices: 1.4770; 1.4745; 1.4635; 1.4500; 1.4445. Continuing these lines until intersection with the toluene-water side of the concentration triangle, abscissas with the following values were obtained graphically, −19.0; −15.4; −3.8; −2.9; −2.6. The value of the abscissas corresponded to conoids distributed in order of removal from the binary system toluene-water.

Let us now examine to what extent the general character of the distribution of the conoids formed corresponded to the observed changes of the refractive index. In order to show this more clearly, the diagram of the system studied is shown schematically on Fig. 4, in which E, T, and W indicate epichlorohydrin, toluene, and water respectively. The scheme shows the region of immiscibility with a series of conoids the distribution of which qualitatively coincides with those found. With such a distribution of conoids, the section line W-n intersects at the beginning of the conoid in which the composition of the epichlorohydrin-toluene liquid phase corresponds to point a_4. It is further apparent from the diagram that the composition of this liquid phase will change correspondingly to points a_3, a_2, and a_1, respectively. The closer the section line W-n approaches the apex W, the more sharply the composition of the liquid phase will change: the relative amount of toluene in it increases, and the amount of epichlorohydrin and water decreases. This conclusion agrees fully with the fact that the solubility of epichlorohydrin is considerably greater in water. For this reason, a greater amount of epichlorohydrin must go into the water layer with the increase of the percent water in the whole ternary system, increasing, in this manner, the relative amount of toluene in the epichlorohydrin toluene layer. If, finally, it is kept in mind that all of the components used, toluene possesses the greatest refractive index, then it becomes very clear that the character of the change in refractive index with the percent water content curves obtained (Fig. 3) agrees completely with that of the distribution of conoids found in the region of immiscibility.

Based on the fact that the mutual solubility of epichlorohydrin in water is greater than in toluene and water, the binary system epichlorohydrin-water can be considered as the subprevailing. Assuming the binary systems to be in such positions as are shown on Fig. 4, it can easily be considered that the character of the distribution of conoids found in the region of immiscibility is in complete accord with R. V. Mertslin's rule.

It must be mentioned that, even though the term "right direction", or "left direction" is purely conditional, the fact of the deviation of conoids from the zero direction is itself very important.

System Phenol—Naphthalene—Water. Timmermans [3], Bautaric and Nabot [4] partially investigated this system, but, since the results of these authors were obtained by scattered experiments, a more complete investigation had to be undertaken. According to literature data and the results of the measurements taken by the authors, the binary systems entering into the given ternary systems having the following characteristics:

1) System phenol-water [5] has a region of interruption of solubility with an upper critical point corresponding to 65.8° the three phased monotectic point is equal to 1.6°, the eutectic composition corresponds to a mixture containing 6.8% of phenol, and the eutectic point is equal to −1.3°.

2) In the system naphthalene-water, the mutual solubility in the studied temperature interval is so small that it is practically impossible to establish the composition and eutectic point. The upper critical temperature of the region of immiscibility was not determined since it was sufficient to know that the critical point of this system was a considerably higher temperature than that in the system phenol-water. The monotectic point was equal to 78.4°.

3) According to Hatcher and Skirrow's [6] data, the eutectic in the system phenol-naphthalene lies at 29.8° and contains 84% of phenol. In order to study the phase composition of the system, the concentration triangle of the composition Ph—N—W (phenol-naphthalene-water) was sectioned with rays having their origin in the various concentration points of the binary system Ph—W and going to the apex N of the triangle. In all, seven sections were studied characterized by phenol contents (in %) in the binary mixture Ph—W: 4.9, 10.1, 25.0, 50.0, 64.7, 75.0, 90.4.

A ternary mixture was synthesized based on these binary mixtures, and the initial starting mixture was heated to a temperature at which complete homogenization of the solution occurred.

Working with these ternary systems, the following aims were sought: a) to determine the surface of crystallization of the three phased monotectic in order to make possible the construction of several limited conoids;

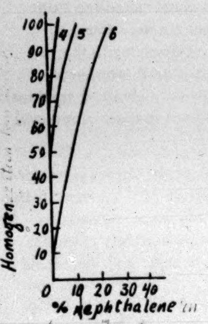


Fig. 6. Polythermic immiscibility curves.

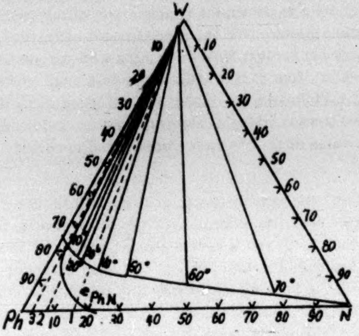


Fig. 7. Projection of the polytherms of the structural diagram of phenol—water—naphthalene showing the positions of the limited conoids and those of the sections chosen (dotted lines 1,2, and 3).

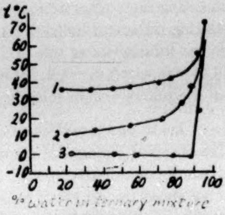


Fig. 8. Change of crystallization point in the verifying sections 1,2, and 3.

b) to construct polythermic curves in the region of the two-phased liquid state for the chosen sections using the well known polythermic method of Alekseev [7] in order to construct a binary curve of the region of immiscibility on the separate isotherms.

TABLE 1

Conoid temperature (°C)	Section 3		Section 6		X
	c_1	a_1	c_2	a_2	
73	55.00	11.25	81.25	14.25	−42.5
70	43.30	14.17	72.10	20.9	−17.33
60	18.40	20.4	42.80	42.9	− 3.27
50	8.00	23.0	23.8	57.0	− 2.68
40	4.50	23.9	13.6	64.8	− 0.81
30	3.00	24.2	9.0	68.5	− 0.27
20	2.40	24.4	7.3	69.5	− 0.18
10	1.60	24.4	5.0	71.2	− 0.17

On the basis of the graphic material obtained, curves of the start of the primary separation of naphthalene crystals from the two-phased liquid state, which corresponded to sections 1,2,3,4, 6, and 7, (Fig. 5), as well as a polythermic curve of the region of immiscibility corresponding to sections 4,5, and 6 (Fig. 6) were constructed. In order to construct a series of limited conoids, the composition points were determined on the graphs corresponding to 70, 60, 50, 40, 30, 10°, and then placed on the corresponding rays of sections 1,2,3,4, and 6. Joining the points with straight lines and continuing them to intersection with the binodal curve corresponding to the given isotherm, seven limited conoids were obtained. In order to quantitatively characterize the distribution of limited conoids in the region of immiscibility, D. N. Tarasenkov's equation $X = \frac{a_2c_1 - a_1c_2}{a_2 - a_1}$ was used where X is the abscissa points of conoid lines with the continuation of one side of the concentration triangle, and a_1c_1 and a_2c_2, the coordinates of the two conjugate liquid phases. Since the composition of the conjugate liquid phases was not determined directly during this method of investigation, two points lying on sections 3 and 6 were used for the calculation of the abscissas for each of the conoids. The concentration of phenol was used for coordinates a_1 and a_2 and the concentration of naphthalene for c_1 and c_2. The numerical material for these calculations is given in Table 1.

The calculated values of the abscissas of intersection points of conoid lines with the continuation of the naphthalene-water side of the triangle show that: 1) the continuation lines of limited conoids do not intersect at the apex of the concentration triangle, and 2) at the corresponding distributions of the binary systems, all of the conoids have a right direction, which corresponds to R. V. Mertslin's rule.

In order to prove the character obtained for the distribution of the conoids, 3 more sections were investigated which had their start in the binary system phenol-naphthalene and are characterized by the following phenol contents (%): 85.0, 93.0, 97.0.

For a better description and subsequent conclusion, the projection of the polytherms of the structural diagrams of Ph-W-N is given in Fig. 7, in which are shown the positions of the limited conoids found, and the lines of the chosen sections (dotted lines 1,2, and 3). In accordance with the position of the limited conoids in these sections, approximately the same form for the curves of the variation of crystallization point of three-phased monotectic with the total weight percent of water in the ternary system must be expected (Fig. 3). Actually, the section lines will intersect a series of conoids corresponding to higher temperatures in relation to the total concentration of water; the closer the figurative point of composition approaches the apex W, the greater must be the increase of the crystallization point of the monotectic in the defined concentration interval.

Such a variation of temperature of the monotectic curve indicates the fact that, in relation to the increase of the concentration of water in the ternary system, because of the large mutual solubility of phenol and water, the phenol-naphthalene layer will be more and more depleted of phenol. Conversely, the relative concentration of naphthalene will increase and therefore, the crystallization point of naphthalene will increase.

Complete polythermic diagrams of the sections studied are not given here; only the relation of the crystallization point of the monotectic to the total concentration of water in the system will be shown. On Fig. 8 it is clearly apparent that the expected temperature variation curves for sections 1 and 2 are proved. The lower curve, corresponding to section 3, is different in form, as well as in character of the monotectic process from the first two, but this difference does not disprove but confirms the character of the distribution of conoids. From the diagrams in Fig. 7, it is apparent that the line of section 3 passes to the left of the conoids upon which the four-phased monotectic process is realized. Therefore, (and this is confirmed by direct observation) initially, the three-phased monotectic exists on this line with phenol crystals. Then, with the concentration of water of about 87%, the section line intersects the conoid of the four phased monotectic (−0.65°) and enters into the region of the monotectic with naphthalene crystals.

Although the positions of the conoids, distributed in the region of the three phased monotectic with phenol crystals is, practically, very difficult to determine, since the temperature interval between the monotectic in the system Ph-W and the four-phased monotectic is only equal to 2.2°, nevertheless, it can be concluded from the diagram of section 3 that there exists one direction for the conoids in the entire system.

System Phenol-Water-Benzoic Acid. According to the literature data [6,8], the upper critical temperature of immiscibility of the binary system benzoic acid-water is equal to 115.5°; the three phased monotectic point is equal to 95°. The eutectic point in the system phenol-benzoic acid is equal to 31° and corresponds to a composition containing 82.5% phenol.

In order to show the character of the crystallization surface of the three phased monotectic in the system phenol-water benzoic acid (Ph-W-B) at 20-80°, 7 sections were investigated. The lines of these sections originated at various concentration points of the binary system Ph-W and passed into the apex B of the concentration triangle Ph-W-B. The phenol content (in %) of the binary mixture (Ph-W) was the following: 3.95, 9.6, 15.1, 25.0, 50.0, 62.6, 75.6.

Ternary mixtures with varying amounts of benzoic acid were synthesized on the basis of these binary mixtures of Ph-W, and then the immiscibility point and the temperature of separation of the first benzoic acid crystals from the two-phased liquid state were measured. The results of these measurements are given in Figs. 9 and 10.

Using the above reported method, a series of limited conoids corresponding to temperatures: 80, 70, 60, 50, 40, 30, and 20° were constructed, and the intersection points of the conoids with the continuation of the side W-B of the concentration triangle Ph-W-P on the abscissa was calculated. Necessary data for this calculation are given in Table 2. Here, c_1 and c_2 are the concentrations of benzoic acid used in sections 2 and 6 and a_1 and a_2 the concentration of phenol in these sections.

TABLE 2

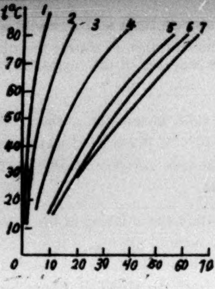
Conoid temperature (°C)	Section 2		Section 6		X
	c_1	a_1	c_2	a_2	
80	16.5	8.0	60.1	25.0	−4.01
70	11.5	8.5	49.0	31.9	−2.12
60	8.3	8.76	40.0	37.5	−1.36
50	6.0	9.0	32.8	43.2	−1.05
40	4.4	9.17	26.0	46.15	−0.95
30	3.0	3.31	19.0	50.63	−0.60
20	2.0	9.4	14.0	53.75	−0.54

It is apparent from Table 2 that the conoids do not intersect at the apex of the concentration triangle, and that the character of the distribution of the conoids is the same as in the previously reported systems.

It must be mentioned that, above 65.8°, the region of immiscibility does not reach the binary system Ph-W; this fact does not introduce any important changes in the character of the distribution of the limited conoids.

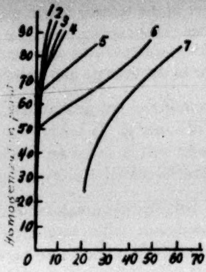
In order to prove the correctness of the distribution found for the conoids, 2 more sections originating in the binary system Ph-B and going to the apex W of the concentration triangle were investigated. The starting binary mixture with benzoic acid had the following phenol content (in %): 82 and 90.

The dotted lines in Fig. 11, designated by the numbers 1 and 2, show the position of the confirming sections. The region of immiscibility is not shown on the diagram, while the limited conoids are bounded by sections 1-7. The eighth



% Benzoic acid in the ternary system

Fig. 9. Curve of the temperature of the start of crystallization of benzoic acid.



% Benzoic acid in the ternary mixture

Fig. 10. Polythermic immiscibility curves.

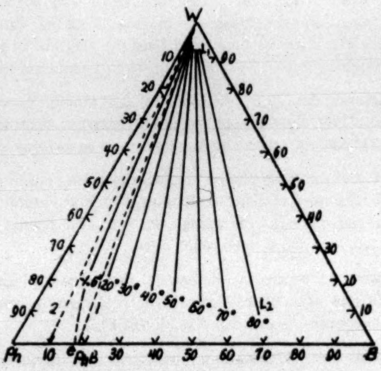
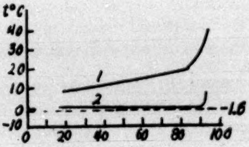


Fig. 11. Distribution of limited conoids in the region of immiscibility and the position of verifying sections 1 and 2.



% water in the ternary mixture.

Fig. 12. Variation of the crystallization point in the verifying sections 1 and 2.

conoids corresponding to −1.6°, is the one upon which the four-phased monotectic process exists.

Even from the diagrams in Fig. 11, it is apparent that section 1 line intersects by means of its continuation from the side Ph-B to the apex W, the conoid corresponding to 20°, and then a series of other conoids with higher crystallization points. Therefore, the curve of the variation of crystallization point of the monotectic with the percent water content in the ternary mixture must have a form analogous to curves 1 and 2 on Fig. 8 in this section.

Section line 2 passes initially through the region of crystallization of the monotectic with phenol crystals, and only at concentrations of water in the ternary mixture equal to 92%, intersects the four-phased monotectic conoid. The results of the measurements for the chosen sections given in Fig. 12, confirm the previous statements.

The fact that the curve of the monotectic with phenol crystals (section 2) falls in the direction of lower temperatures indicates that, in this system, in a similar manner to the system phenol-water-naphthalene, a single direction for the limited conoids exists.

The relatively small rise of the curve in the direction of higher temperatures with these sections, is explained by the fact that the region of immiscibility is less developed in this system than in that of phenol-water-naphthalene. For this reason, conoids corresponding to higher temperatures are intersected sooner by the binodal curve then by the section lines.

This character of distribution of conoids makes it possible to theoretically predict the qualitative changes in conjugate phases and the behavior of certain systems during crystallizations for any system in which chemical compounds or solid solutions do not arise.

SUMMARY

1. The theoretical conclusions of R.V. Mertslin on the single direction of conoids in the ternary system with a single region of immiscibility for the two binary systems were proved correct for the systems studied: epichlorohydrin-toluene-water, phenol-naphthalene-water, and phenol-water-benzoic acid.

2. It was shown that the character of the distribution of conoids of the two phased liquid state is retained up to the crystallization point, i.e., it embraces the limited conoids which are iso thermal crystallization lines in the region of immiscibility.

3. The hypothesis of D.N. Tarasenkov on the joining of the continuation lines of the conoids at one of the apexes of the concentration triangle was disproved.

4. The results obtained gave a basis for the general qualitative evaluation of structural diagrams and enable methods for the crystallization of certain ternary systems to be determined.

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COMPLEX COMPOUNDS OF NICKEL WITH DIMETHYLGLYOXIME

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The reaction of the nickel ion with dimethylglyoxime has been known for a long time, but up to now, the question of the structure of the soluble complex compound obtained by the reaction of nickel with dimethylglyoxime in alkaline medium remains unanswered. Feigl [1] considers that the soluble complex is a compound of dimethylglyoxime with tetravalent nickel.

Hooreman [2] states that dimethylglyoxime gives two colored complexes with tetravalent nickel; in one the ratic of nickel to dimethylglyoxime is equal to 1:2, in the other, 1:4.

Another view is held by Babko [3]. He believs that nickel is divalent in this complex and is combined with an unstable product of the oxidation of dimethylglyoxime. The composition of the complex corresponds to a ratio of nickel to dimethylglyoxime equal to 1:2, for a small excess of the oxidizing agent, and 1:3 for a large excess.

It was observed that, upon mixing solutions of nickel salts with those of dimethylglyoxime in the presence of concentrated ammonia, no precipitate is formed, and the solution is gradually colored red. A colored complex compound is formed, it is believed, the study of whose properties is of interest from a theoretical as well as from a practical viewpoint.

The system nickel sulfate-dimethylglyoxime-aqueous ammonia solution was studied. The method of Ostromyslensky-Dzhob, i.e., the study of the mixture of solutions of nickel sulfate and dimethylglyoxime of identical polarity under various volume ratios at a constant total volume, could be used to determine the composition of the colored compound. But this method can only give a one sided characterization of the system, since it detects the existence of only one complex compound.

Babko [5] further developed the method for the investigation of solutions of complex compounds and offered to study more widely the properties of a similar type of multicomponent system. The system investigated can be schematically described in the form of a triangle (Fig. 1). Using Babko's method, the properties of the system were studied by means of sections 1-2, 3-4, and 5-6. The optical density of the mixture was chosen as the property of the system.

EXPERIMENTAL

0.0044 molar solutions of nickel sulfate and dimethylglyoxime were used for the investigation.

During the preparation of the mixture, it was found that the reaction forming the colored complex proceeds with time.

The results of the observation are shown on Fig. 2.

During the first 80 hours the optical density of the solution (the thickness of the absorption layer was 5 cm) increased continually, acquired a maximum, and was constant for the following 60 hours, and then very slowly decreased. All of the subsequent observations were conducted after 4-5 days (100-120 hours).

At first, mixtures with changing concentration of nickel sulfate and dimethylglyoxime and a constant concentration of aqueous ammonia were investigated in series of experiments. Sections of the type 1:2 on Fig. 1 correspond to those. Upon the preparation of mixtures of solutions of nickel sulfate and dimethylglyoxime of various volume ratios, the total volume remained constant. The total molarity of the nickel sulfate and dimethylglyoxime in the experiments was equal to $8.8 \cdot 10^{-4}$ M.

Three series of mixtures were investigated. In each series, the concentration of ammonia was changed. In the first series, the total molarity of the ammonia was 3.25, in the second, 4.37, and in the third, 5.58. Within five days after the preparation of the mixture, the optical density of the solution was measured on a Moskin photocolorimeter with yellow filters. The variation of the optical density with the ratic of the volumes of nickel sulfate and dimethylglyoxime is described on Fig. 3 by three curves. All of the curves have a maximum at a ratio

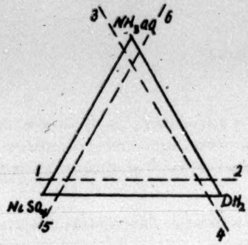

Fig. 1. Scheme of the directions of the sections in the system nickel sulfate-dimethylglyoxime-aqueous ammonia solution.

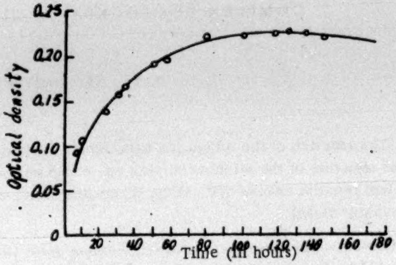

Fig. 2. Curve of the change in color of the complex with time.

of volumes of nickel sulfate and dimethylglyoxime, equal to 1:3, which corresponds to the same ratio for the number of molecules.

Then a mixture with a constant concentration of nickel sulfate ($8.8 \cdot 10^{-5}$ moles) and a changing concentration of dimethylglyoxime (from $2.64 \cdot 10^{-4}$ to $1.3 \cdot 10^{-3}$ moles), was investigated, corresponding to section 3-4 on Fig. 1. The concentration of ammonia in all of these experiments was constant and was equal to 3.36 moles. The variation of the optical density of the solution with the concentration of dimethylglyoxime for this case is shown on Fig. 4.

The system nickel sulfate-dimethylglyoxime-aqueous ammonia solution was also investigated at section 5-6 (Fig. 1). In this case, the concentration of dimethylglyoxime was kept constant ($8.8 \cdot 10^{-5}$ moles), and the concentration of nickel sulfate was changed (from $4.4 \cdot 10^{-6}$ to $3.52 \cdot 10^{-4}$ moles). The concentration of ammonia in all experiments was 3.36 moles. The results of the measurement of the optical density of these solutions is shown on Fig. 5.

DISCUSSION OF RESULTS

The optical data obtained by the investigation of the systems of nickel sulfate-dimethylglyoxime-aqueous ammonia made is possible to make a suggestion on the nature of the colored complex which formed. According to the authors, the compound of nickel and dimethylglyoxime in ammoniacal medium, is the product of the reaction of dimethylglyoxime, bivalent nickel, and the oxygen of the air which is the oxidizing agent. This is confirmed by experiments conducted with solutions prepared with redistilled water saturated with nitrogen. Such solutions, sealed in ampoules, remained practically colorless even on prolonged standing. When these ampoules were opened the solution colored rapidly, and in certain of these where the concentration of nickel was high, a precipitate formed. Apparently, the oxygen of the air oxidizes the dimethylglyoxime, and the latter reacts with bivalent nickel.

The properties of the solutions of the colored complex compound of nickel with dimethylglyoxime reported is essentially different from those reported by Feigl [1], since, for example, by the oxidation of the solutions obtained, neither a red brown precipitate nor iodine from potassium iodide solutions was formed.

The formation of the colored complex compound, as was stated above, does not occur with the complete absence of oxygen in the water and occurs in the presence of even small amounts of oxygen after some time; for this reason the above reaction may be used to detect dissolved oxygen in water and in aqueous solutions.

The curve in Fig. 2 shows the change of the optical density of the mixture containing nickel sulfate, dimethylglyoxime, and ammonia with the time. The optical density passes through very flat maximum and then decreases which indicates the simultaneous occurence of at least 2 processes in the system, the formation of the complex compound and very slowly, its decomposition. It must be mentioned that the solutions keep their color even after several months.

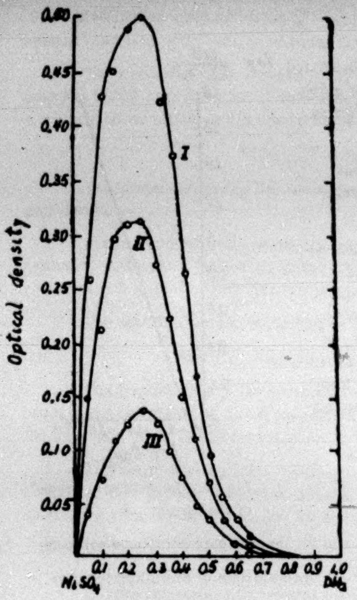

Fig. 3. Volume ratio of solutions of nickel sulfate and dimethylglyoxime according to section 1-2 and the optical density.

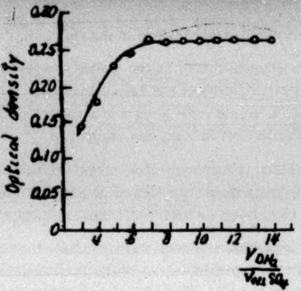

Fig. 4 Variation of the optical density with the concentration of dimethylglyoxime according to section 3-4.

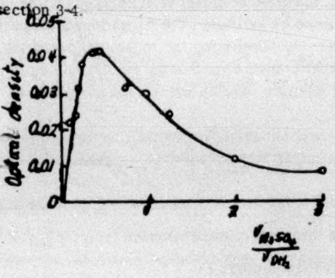

Fig. 5. Change in the optical density of the solution of the system nickel sulfate-diemethylglyoxime according to section 5-6.

On curves I, II, III (Fig. 3) for the system nickel sulfate dimethylglyoxime-ammonia, a maximum optical density can be found at ratios of nickel sulfate to dimethylglyoxime equal to 1: 3, which apparently, corresponds to the composition of the compound formed. The curves obtained are not symmetrical. Branches of the curve to the right of the maximum pass considerably more abruptly downward than those to the left of it, and at ratios of the number of molecules equal to 1:1, a clear inflexion can be seen on the curve. Such a form of the curve, indicates, according to the authors, the existence in addition to the colored complex (with a molar ratio of the components, 1:3), another, colorless one (with a suggested ratio of the reacting components 1:1). The same conclusion, as it will be shown below, is arrived at by the study of the systems with a constant concentration of dimethylglyoxime.

From the curves I, II, III placed on Fig. 3, it is apparent that, with the change of the concentration of the ammonia, the position of the maximum does not change, only its height changes. The highest maximum corresponds to a mixture in which the concentration of ammonia is 3.52 molar, the lowest maximum, with a concentration of 5.58 molarity. Therefore, with the increase of the concentration of ammonia, the degree of dissociation of the complex increases. This phenomenon can be explained if it is assumed that the following equilibrium occurs in the solution:

$$Ni(NH_3)_6^{2+} + 3DH^{0-} \rightleftarrows [NiDH_3^0]^- + 6NH_3 \qquad (1)$$

where DH^{0-} is the oxidized form of dimethylglyoxime. Supplementary proof of the existence of such an equilibrium in the system studied will be given below.

Upon keeping the initial concentration of nickel sulfate constant and continually increasing the concentration of dimethylglyoxime (in ammonia solution), the curve of the optical density first rises sharply, then becomes almost parallel to the abcissas, and approaches a definite value of the optical density (Fig. 4). This value of the optical density corresponds to practically complete conversion of the nickel salt to the complex compound, equilibrium (1) is practically completely shifted to the right.

The compounds formed in the system are found in the partially dissociated state. If the dissociation of the compounds were insignificant, then the graph, shown on Fig. 4, would have been a broken line with an inflexion occurring at the composition of the complex compound.

Nevertheless, the compounds of nickel with dimethylglyoxime possess a sufficiently great stability, since if an extensive dissociation were present, there would have been no horizontal branch found on Graph 4.

The molar extinction coefficient of the compound formed was calculated from the determined values of the optical density (Fig. 4). It was assumed that practically all of the nickel sulfate found in the solution had been converted into the complex compound. By investigating the graph in Fig. 4, the ratio of nickel to dimethylglyoxime in the colored complex can once more be verified. The "logarithmic graph" method was used for this purpose. By substituting the concentrations of the reaction components from the experimental data into the equilibrium equation expressing the constants of the reaction forming the colored complex, we obtain:

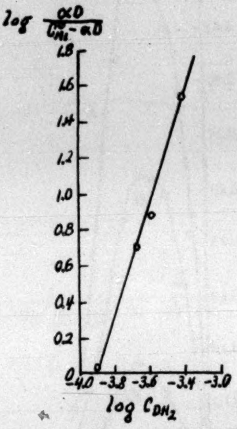

Fig. 6. "Logarithmic graph" of the system.

$$\frac{\alpha D C^{0\,6}_{NH_3}}{(C^0_{Ni} - \alpha D)\,(C^0_{DH} - 3\alpha D)^3} = K_e$$

where D is the optical density; $\alpha = \frac{1}{El}$ (E is the molar extinction coefficient for the complex compound solution) l is the thickness of the absorption layer: C^0_{DH}, C^0_{Ni} and $C^0_{NH_3}$, the initial concentrations of dimethylglyoxime, nickel, and ammonia.

The product αD is equal to the concentration of the colored complex in the solution.

By rearranging the expression for the equilibrium constants and transforming it into logarithms, a relation is obtained expressed by a straight line, if the abscissas are made to correspond to the logarithmic ratio of the concentration of the colored complex to the equilibrium concentration of nickel and the equilibrium concentration of dimethylglyoxime, to the ordinates.

$$\log \frac{\alpha D}{C^0_{Ni} - \alpha D} = \log K - 6 \log C^0_{NH_3} + 3 \log (C^0_{DH} - 3\alpha D).$$

The tangent of the angle of inclination characterizes the coordination number, which was found to be equal to 3 (Fig. 6).

Therefore, the same result for the composition of the complex is found by the logarithmic graph method as by Ostromyslenky-Dzhob's method.

The section, cut off by the straight line on the ordinates at an equilibrium concentration of dimethylglyoxime equal to 1 molar, is directly related to the value of the equilibrium constant. The value of the logarithm of the equilibrium constant calculated from the data given in Fig. 6, was found to be equal to 14.8. This value was confirmed by the calculation of the equilibrium constant from the optical data from mixtures with varying concentrations of dimethylglyoxime and nickel sulfate (with different concentrations of ammonia)(Fig. 3).

The values ≈14.1 and 14.9 are obtained in this case for the logarithm of the equilibrium constant, which is close to that calculated above.

The instability constant of the colored complex was calculated, which is related to the simple ratio of the equilibrium constant of reaction (1) and the instability constant of the complex ion $Ni(NH_3)_6^{2+}$

$$K_{instability} \frac{K_{instability\ Ni(NH_3)_6^{2+}}}{K_e}$$

The instability constant of $Ni(NH_3)_6^{2+}$, according to Bjerrum [4], is equal to $1.8 \cdot 10^{-9}$. The instability constant of the colored complex was found to be equal to $3 \cdot 10^{-23}$.

The curve in Fig. 5, expressing the relation of the optical density to the concentration of nickel sulfate (at constant initial concentration of dimethylglyoxime in the solution), shows that the maximum optical density approaches a molar ratio of nickel to dimethylglyoxime equal to 1:3. The following reaction occurs in the solution:

$$Ni(NH_3)_6^{2+} + 3DH^{0-} \rightleftarrows Ni(DH^0)_3^- + 6NH_3$$

On further increasing the concentration of nickel sulfate the optical density of the solution decreases and approaches zero.

If other complex compounds did not exist in the solution, then the optical density would have remained almost constant. Apparently the excess nickel sulfate reacts with the colored complex and converts it into another uncolored complex with a smaller coordination number.

The reaction occurs, evidently, by the equation:

$$Ni(DH^0)_3^- + 2Ni(NH_3)_6^{2+} = 3NiDH^0(NH_3)_x^+ + (12-3x)NH_3$$

The composition of the complex compound with a ratio of nickel to dimethylglyoxime of 1:1 was adopted because the compound of nickel and dimethylglyoxime with a ratio of 1:2 is colored. In addition, the position of the inflexion point on the curves in Fig. 3 favors this view.

Therefore, a many sided investigation of the system nickel sulfate-dimethylglyoxime-ammonia leads to the conclusion that at least two complexes are present in the system; one is colored which has a ratio of nickel to dimethylglyoxime equal to 1:3, and the other is colorless with a ratio, evidently, equal to 1:1.

SUMMARY

1. The formation of a colored complex was discovered upon the reaction of nickel sulfate with dimethylglyoxime in an ammoniacal medium in the presence of oxygen from the air.

2. The composition of the colored complex was determined by a physico-chemical method of analysis and corresponded to a ratio of nickel to dimethylglyoxime equal to 1:3.

3. The reaction forming the colored complex occurs with time.

4. In addition to the colored complex compound, a colorless one exists in the system with a molar ratio of nickel to dimethylglyoxime equal to 1:1.

5. On the basis of the study of the reaction between the complex compounds formed and the ammonia, the corresponding equilibrium constant and instability constant of the complex compound of nickel with dimethylglyoxime were calculated.

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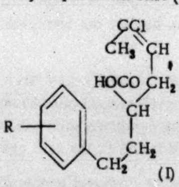
SYNTHESIS OF POLYCYCLIC HYDROAROMATIC KETONES

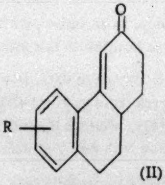
VII. 6- and 7-METHOXY-3-KETO-1,2,3,9,10,10a-HEXAHYDROPHENANTHRENES

G. T. Tatevosyan, P. A. Zagorets and A. G. Vardanyan

Previously, it was shown [1] that sulfuric acid hydrolysis and subsequent double cyclization of substituted γ-phenylbutyric acids with a γ-chlorocrotyl group in the α-position to the carboxyl(I) leads to the formation of substituted 3-ketohexahydrophenanthrenes (II):



(I)



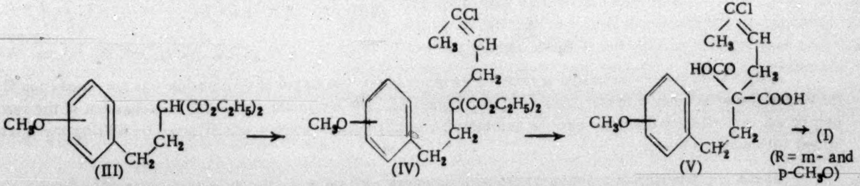
(II)

I was also found that the presence and position of a methyl group in the aromatic nucleus of the starting acid did not have any significant effect on the tendency of the acid to cyclize and on the yield of the reaction products [2].

It seemed of interest to investigate the analogous transformation of acids of this series with a methoxyl group in the aromatic nucleus, which is, as is known, a considerably stronger expressed ortho and para orientating substituent than the methyl group.

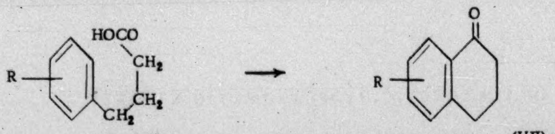
The expected cyclization products were ketomethoxyhexahydrophenanthrenes (II. R = 6- and 7-CH_3O) which in themselves can be of interest as starting substances for the synthesis of compounds related in structure to Doisynolic acid, as well as for the preparation of analgesically active amino derivatives of partially hydrogenated phenanthrene.

The above acids (I. R = m- and p-CH_3O) were prepared from the corresponding β-anisylethylbromides and 1,3-dichlorobutene-2 by means of the malonic acid via compounds (III), (IV), and (V):



The ability of γ-phenylbutyric acids to intramolecularly acylate depends to a considerable degree on the nature and position of the substituents found in the aromatic nucleus.

According to certain literature data [3], γ-(m-anisyl)butyric acid(VI. R = m-CH_3O) readily undergoes intramolecular acylation and forms 6-methoxytetralone-1 (VII. R = 6-CH_3O) by the action of sulfuric acid and other cyclizing agents:



(VI) (VII)

On the other hand, Krollpfeiffer and Schäfer [4] did not obtain any 7-ethoxytetralone-1 (VII, R = 7-CH_3O) when they tried to cyclize γ-(p-anisyl)butyric acid (VI, R = p-CH_3O) by heating with sulfuric acid; the starting material was completely sulfonated. This substance can not only be explained by the facile sulfonation of the aromatic ring in the starting acid, but also by the deactivating effect of the methoxyl group upon cyclization. The latter view is confirmed by the fact that the same γ-(p-anisyl)butyric acid cyclizes only to an extent of 61.5 % [5] by the action of liquid hydrogen fluoride, while the unsubstituted acid (VI, R = H) from tetralone-1 (VII, R = H) in a yield of 92.0% [6] under the same conditions.

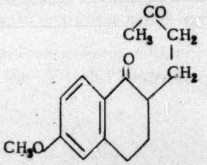
Therefore, the methoxy group, as an ortho-para-orienting substituent, hinders the intramolecular acylation which occurs in the meta position in relation to this group.

From a study of the reported literature data, it was expected that sulfuric acid hydrolysis and cyclization of α-(3-chlorocrotyl)-γ-(m-anisyl)butyric acid (I, R = m-CH_3O) into 3-keto-7-methoxyhexahydrophenanthrene (II, R = 7-CH_3O) would occur smoothly, whereas it could be expected that the complete sulfonation of the isomeric acid (I, R = p-CH_3O) was probable, since both are γ-(p-anisyl)butyric acids substituted in the side chain.

On the other hand, the presence of a substituent in the α-position to the carboxyl group, which favored, according to other observations [7], cyclization of γ-arylbutyric acids, gave a basis for expecting that the intramolecular acylation will occur at comparatively lower temperatures which do not favor sulfonation.

3-Keto-7-methoxyhexahydrophenanthrene (II, R = 7-CH_3O), characterized in the form of 2,4-dinitrophenylhydrazone, was obtained in 57% yield by the reaction of α-(3-chlorocrotyl)-γ-(m-anisyl)butyric acid (I, R = m-CH_3O) with sulfuric acid (d 1.78) at 60-75°.

Under more forcing conditions, the sulfonation of the starting acid was greatly intensified which strongly decreased the yield of tricyclic ketone, while gentler conditions (moderate and shorter heating of the reaction mixture) resulted in a reaction product which was a mixture of the final substance and the bicyclic diketone (VIII) formed as a side product:



(VIII)

A still more sharply expressed separate occurrence of the two stages of cyclization was previously found during the preparation of ketones with the chrysene cyclic system [8]. The intramolecular aldol condensation of the remaining part of the intermediate diketone into the ketomethoxyhexahydrophenanthrene was effected by boiling the mixture obtained with aqueous alkali.

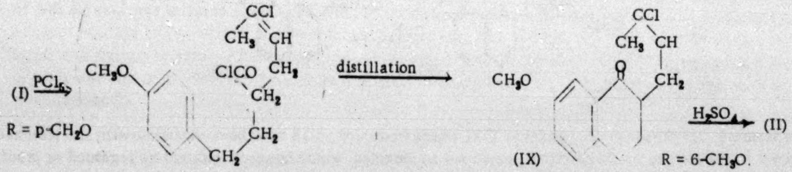
There, the presence of a methoxyl group in the meta position, actually, does not prevent cyclization. Nevertheless it must be mentioned that the yield of the cyclization product (57%) was somewhat lower than the yields obtained with the unsubstituted acid [1] or acids methylated in the aromatic ring of the same series [2] (60-80%), which, evidently, must be explained by comparatively easy sulfonation of the methoxylated aromatic ring.

Upon attempting to cyclize α-(3-chlorocrotyl)-γ-(p-anisyl)butyric acid (I, R = p-CH_3O) with sulfuric acid (d 1.74) at 65-70°, it was almost completely sulfonated, and only a very small amount of a substance which proved to be 3-keto-6-methoxyhexahydrophenanthrene (II. R = 6-CH_3O) could be isolated from the reaction mixture.

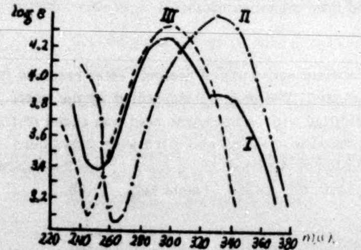
In isolated cases, substituted γ-phenylbutyric acids are cyclized with sulfuric acid at lower temperatures. Thus, V. M. Rodionov and N. N. Suvorov showed [9] that the triethyl ester of α-phenyl-β-benzylethane-α,β,β-tricarboxylic acid readily cyclized into 3,3-dicarbethoxy-2-phenyltetralone-1 even at room temperature on a two day standing with concentrated sulfuric acid. Attempts to cyclize the acid (I. R = p-CH_3O) under these conditions were found to be unsuccessful; only traces of the tricyclic methoxyketone were formed in this case.

In order to convert the acid (I. R = p-CH_3O) into 3-keto-6-methoxyhexahydrophenanthrene, Krollpfeiffer and Schäfer's discovery [4] which showed that γ-(p-anisyl)butyric acid chloride readily cyclized upon vacuum distillation with the cleavage of hydrogen chloride, was applied.

2-(γ-Chloro)crotyl-7-methoxytetralone-1 (IX) was formed in 80% yield by the distillation of the acid chloride (I. R = p-CH_3O) prepared by the reaction of the acid with phosphorus pentachloride. The latter was an o,o'-substituted tetralone and did not form a semi-carbazone even upon prolonged standing with semicarbazide solution.



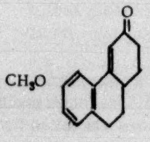
It could have been assumed that ketone (IX), like other γ, δ-unsaturated δ-chloroketones [10], would be subjected to hydrolysis by sulfuric acid followed by cyclization under mild conditions which would practically exclude the possibility of excessive sulfonation. Actually, 3-keto-6-methoxyhexahydrophenanthrene (II. R = 6-CH_3O) was formed in a yield of 63.5% by the action of cold sulfuric acid (d 1.74) on ketone (IX).



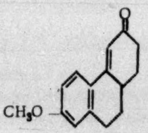
Absorption spectra of the methoxyketones

The absorption spectra of the methoxy ketones synthesized, as well as that of the unsubstituted 3-ketohexahydrophenanthrene obtained previously [1,11] were obtained by the method of photographic spectrophotometry. The dimming of the light rays was accomplished by rotating the sector with varying angles of exposure. The spectrograms were photomerized on the MF-2 microphotometer. Ethyl alcohol, carefully purified and optically transparent in the region investigated, served as the solvent.

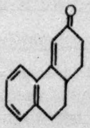
The ultraviolet absorption curves of three investigated ketones (Fig. 1) are similar in their form and position of the maximum to those of benzalacetone and compounds having the system of conjugated double bonds of the latter in their molecules [12]. The absorption curve of the 7-methoxy derivative, in comparison to those of the other two ketones, is shifted strongly toward the longer wave lengths; its maximum differs from that of the other two curves by 35-40 mμ. This phenomenon can be explained by the presence of the para methoxyl group, which causes a shift of the electron density in the direction of the carbonyl group from the methoxyl leading to an increase in length or effective configuration of the system of double bonds.



I



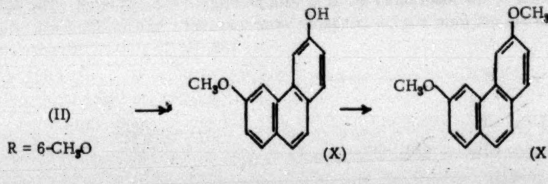
II



III

On the curve of the 6-methoxy derivative, in whose molecule the possibility of such a shift is excluded by the presence of a meta methoxyl group, the maximum coincides with that of the unsubstituted 3-ketohexahydrophenanthrene. However, there is a small bulge on the lower part of this curve. Since this bulge coincides in wavelength with the maximum in the curve of the 7-methoxy derivative (320-325 mμ), the above circumstance can be explained by the presence of the 7-methoxy derivative as an impurity in the investigated 3-keto-6-methoxyhexahydrophenanthrene preparation. The presence of this impurity may be explained by the formation of a small amount of m-bromoanisole during the bromination of the starting material, anisole, to give p-bromoanisole.

In view of the fact that 3-keto-6-methoxyhexahydrophenanthrene was prepared by a method somewhat different from that used for the synthesis of the other ketones of this series, and because the 7-methoxy isomer was assumed to be present in the investigated preparation of this substance, it was subjected to dehydrogenation with sulfur in order to prove its structure and possibly establish the presence of the isomer. 3-Hydroxy-6-methoxyphenanthrene (X) was obtained which was then methylated to 3,6-dimethoxyphenanthrene (XI) [13].



(II)
R = 6-CH$_3$O

(X)

(XI)

The isomeric 2,6-dimethoxyphenanthrene [13], whose formation could have been expected with the presence of the 7-isomer in the starting methoxy ketone, could not be detected, which however, can not be regarded as proof of its complete absence.

EXPERIMENTAL

The starting β-(m-anisyl)ethylbromide was prepared from m-iodoanisole [14] by the action of ethylene oxide oxide on its magnesium derivative, followed by reaction of the β-(m-anisyl)ethyl alcohol with phosphorus tribromide [3b]. β-(p-Anisyl)ethyl bromide [15] was obtained by the same method from p-bromoanisole.

β-(m-Anisyl)ethylmalonic ester (III. m-CH$_3$O)

98 g of β-(m-anisyl)ethyl bromide was added gradually to the sodium derivative of malonic ester prepared in 150 ml of absolute alcohol from 11.5 g of sodium and 80 g of malonic ester. The mixture was boiled on the water bath for 4 hours, a large part of the alcohol was distilled off, water acidified with hydrochloric acid was added to the residue, the product was extracted with ether, the ether solution was washed with water, and dried with anhydrous sodium sulfate. After the removal of the ether, the residue was twice vacuum distilled. 67 g (50% of the theoretical amount) of an almost colorless oil with b.p. 175-180° at 3 mm; d_4^{20} 1.1146; n_D^{20} 1.4960. Found MR$_D$ 77.05. $C_{16}H_{22}O_5$. Calculated 77.43.

0.1058 g substance: 0.2547 g CO_2; 0.0762 g H_2O. 0.1044 g substance: 0.2496 g CO_2; 0.0712 g H_2O. Found %: C 65.65, 65.20, H 8.00, 7.57. $C_{16}H_{22}O_5$. Calculated %: C 65.31; H 7.48.

β-(p-Anisyl)ethylmalonic ester (III. p-CH$_3$O)

230 g (78.23% of the theoretical amount) of the previously [16] reported ester was obtained in an analogous manner from 180 g of malonic ester, 23 g of sodium, and 215 g of β-(p-anisyl) ethylbromide in 380 ml of absolute alcohol. The preparation obtained had the following properties: b.p. 174-176° at 2 mm; d_4^{12} 1.1003; n_D^{12} 1.4999. MR$_D$ 78.62; calculated 77.43.

[β-(m-Anisyl)ethyl(γ-chloro)crotyl] malonic ester (IV. m-CH$_3$O)

60 g of β-(m-anisyl)ethylmalonic ester was added to a solution of sodium alcoholate prepared from 4.7 g of sodium in 64 ml of absolute alcohol. The mixture was heated for a half-hour on the water bath. Upon cooling, 27.5 g of freshly redistilled 1,3-dichlorobutene-2 was added dropwise with stirring. The mixture was boiled for 4 hours and half of the alcohol used initially was distilled off; the residue in the flask was cooled and diluted with acidified water until complete solution of the precipitated salts; the reaction product was dissolved in ether, the ether solution was washed with water, and dried with anhydrous sodium sulfate. After the removal of the ether, the

residue was vacuum distilled. 67.5 g (86.5% of the theoretical amount) of a light-yellow, thick oil boiling at 205-209° at 3 mm was obtained: d_4^{20} 1.1246; n_D^{20} 1.5087. Found MR_D 101.50. $C_{20}H_{27}O_5Cl$. Calculated 100.31.

0.1009 g substance: 0.0374 g AgCl; 0.1034 g substance: 0.393 g AgCl. Found %: Cl 9.17, 9.40. $C_{20}H_{27}O_5Cl$. Calculated %: Cl 9.28.

[β-(p-Anisyl)ethyl-(γ-chloro) crotyl] malonic ester (IV. p-CH_3O)

328 g (85% of the theoretical amount) of an almost colorless thick liquid with b.p. 221-223° at 6 mm was obtained by the above-reported method from 23 g of sodium, 312 ml of absolute alcohol, 294 g of β-(p-anisyl) ethylmalonic ester, and 135 g of dichlorobutene: d_4^{18} 1.1349; n_D^{18} 1.5123. Found MR_D 101.11. $C_{20}H_{27}O_5Cl$. Calculated 100.31.

0.1094 g substance: 0.0412 g AgCl. 0.1140 g substance: 0.0430 g AgCl. Found %: Cl 9.34, 9.34. $C_{20}H_{27}O_5Cl$. Calculated %: Cl 9.28.

[β-(m-Anisyl)ethyl-(γ-chloro)crotyl]malonic acid (V. m-CH_3O)

A mixture of 68.3 g of the disubstituted malonic ester (IV. m-CH_3O), 22.7 g of sodium hydroxide, and 320 ml of 90% alcohol was refluxed for 5 hours with 200 ml of water, and the alcohol distilled off completely. The cooled aqueous solution was acidified, the precipitated product dissolved in ether, the ether solution washed with water, and dried with sodium sulfate. After the removal of the ether, 52 g (89.2% of the theoretical amount) of light yellow crystals was obtained. Recrystallized from a mixture of benzene and alcohol, colorless crystals with m.p. 138-139° were obtained.

0.1002 g substance: 0.0450 g AgCl. 0.1004 g substance: 0.0468 g AgCl. Found %: Cl 11.11, 11.06. $C_{16}H_{19}O_5Cl$. Calculated %: Cl 10.87.

[β-(p-Anisyl)ethyl-(γ-chloro)crotyl]malonic acid (V. p-CH_3O)

99.5 g (77.73% of the theoretical amount) of the impure light yellow crystalline product was obtained by the saponification of 150 g of the disubstituted malonic ester (IV. p-CH_3O) by a solution of 50 g of sodium hydroxide in 700 ml of 90% alcohol. After recrystallization from hot water, the acid was obtained in the form of colorless crystals with m.p. 136-137°.

0.1102 g substance: 0.0498 g AgCl. 0.1066 g substance: 0.0480 g AgCl. Found %: Cl 11.18, 11.14. $C_{16}H_{19}O_5Cl$. Calculated %: Cl 10.87.

α-(3-Chlorocrotyl)-γ-(m-anisyl)butyric acid (I. R = m-CH_3O)

50.3 g of the unrecrystallized dibasic acid (V. m-CH_3O) was decarboxylated by heating until the evolution of carbon dioxide ceased. The oil which formed was vacuum distilled. 40 g (91.9% of the theoretical amount) of a light-yellow, very viscous liquid with b.p. 207-210° at 5 mm was obtained: d_4^{22} 1.1514; n_D^{20} 1.5354. Found MR_D 76.44. $C_{15}H_{19}O_3Cl$. Calculated 75.44.

0.1056 g substance: 0.0536 g AgCl. 0.1041 g substance: 0.0536 g AgCl. Found %: Cl 12.56, 12.73. $C_{15}H_{19}O_3Cl$. Calculated %: Cl 12.56.

α-(3-Chlorocrotyl)-γ-(p-anisyl)butyric acid (I. R = p-CH_3O)

62.2 g (89.8% of the theoretical amount) of a viscous yellowish-green liquid, boiling at 192-193° at 3 mm was obtained by the decarboxylation of 80 g of the crude dibasic acid (V. p-CH_3O); d_4^{18} 1.1595; n_D^{18} 1.5396. Found MR_D 76.39. $C_{15}H_{19}O_3Cl$. Calculated 75.44.

0.1098 g substance: 0.0550 g AgCl. 0.1078 g substance: 0.0548 g AgCl. Found %: Cl 12.40, 12.58. $C_{15}H_{19}O_3Cl$. Calculated %: Cl 12.56.

3-Keto-7-methoxy-1,2,3,9,10,10a-hexahydrophenanthrene (II. R = 7-CH_3O)

a) 30 ml of sulfuric acid (d 1.78) was added gradually with stirring and cooling with ice water to 5 g of the substituted butyric acid. The cherry-red solution was left to stand at room temperature for a half hour until foaming caused by the voluminous evolution of hydrogen chloride ceased, and then was heated for 3 hours at 60-65° on the water bath in a stream of carbon dioxide, and left to stand over night. On the following day, the reaction mixture was poured on ice, the precipitated oil-like substance was dissolved in ether, the ether solution washed thoroughly with dilute alkali, then with water, and dried with sodium sulfate. Upon the acidification of the alkaline wash solution, it clouded slightly but the formation of an insoluble substance did not occur. After the removal of the ether, 2.9 g of a yellowish crystalline substance remained, which was recrystallized from alcohol (boiling with carbon). 2.3 g (57% of the theoretical amount) of colorless crystals with m.p. 114-115° was obtained.

0.1018 g substance: 0.2948 g CO_2; 0.0682 g H_2O. 0.1004 g substance: 0.2899 g CO_2; 0.0650 g H_2O. 0.2179 g substance: 0.2305 g AgI. Found %: C 78.96, 78.74; H 7.18, 7.19; CH_3O-group 13.50. $C_{14}H_{13}O(OCH_3)$. Calculated %: C 78.94; H 7.02; CH_3O-group 13.59.

The 2,4-dinitrophenylhydrazone, obtained by heating 0.3 g of the ketone and 0.26 g of dinitrophenylhydrazine in 40 ml of alcohol, formed dark-red light needles with m.p. 219-220° after recrystallization from a mixture of chloroform and alcohol.

0.1010 g substance: 13.5 ml N_2 (23°, 678 mm). Found %: N 13.75. $C_{21}H_{20}O_5N_4$. Calculated %: N 13.72.

b) 5 g of the acid (I. R = m-CH_3O) was treated with 30 ml of sulfuric acid (d 1.78) under conditions analogous to those of the previous experiment, with the only difference being that, during the heating of the reaction mixture, the bath temperature was kept within the limits of 30-50°, and the mixture was processed directly after the 3 hour heating. 2.7 g of yellowish oily crystals was obtained, colorless, with m. p. 56-60° after recrystallization from alcohol.

0.1012 g substance: 0.2796 g CO_2; 0.0712 g H_2O. Found %: C 75.35; H 7.81.

The product, a mixture of the ketomethoxyhexahydrophenanthrene with the intermediate bicyclic diketone, was boiled for 2 hours with 20 ml of a 20% sodium hydroxide solution and then twice recrystallized from alcohol (boiling with carbon). The colorless crystalline substance obtained had a m.p. 114-115° (3-keto-7-methoxyhexahydrophenanthrene).

Action of sulfuric acid on α-(3-chlorocrotyl)-γ-(p-anisyl) butyric acid.

15 g of the acid (I. R = p-CH_3O) was treated with 80 ml of sulfuric acid (d 1.74) under the above-reported conditions (see experiment a). Upon mixing the sulfuric solution with ice water, a very small amount of a solid substance formed. The substance was dissolved in ether, the ether solution was washed with dilute alkali, then with water, and dried with sodium sulfate. The light yellow crystals remaining after the removal of the ether melted at 110-111° after recrystallization from alcohol (boiling with carbon). A mixed sample with 3-keto-6-methoxy-1,2,3,9,10,10a-hexahydrophenanthrene (see below) melted at the same temperature.

A two weeks' standing at room temperature of a mixture of 10 g of the acid (I. R = p-CH_3O) and 50 ml of sulfuric acid (d 1.84) also led to the formation of water-soluble sulfonic acids; only traces of the tricyclic methoxyketone were obtained.

2-(γ-Chloro)crotyl-7-methoxytetralone-1 (IX)

134 g of phosphorus pentachloride was added in small portions with stirring to a solution of 184 g of the acid (I. R = p-CH_3O) in 300 ml of dry benzene in a distillation flask. At the end of the violent reaction, the mixture was heated on the water bath for a half hour; part of the benzene was distilled off during this heating. The water bath was removed and the remaining benzene, as well as the phosphorous oxychloride formed during the reaction, were distilled off at atmospheric pressure. The distillation of the residue in vacuum was accompanied by a voluminous evolution of hydrogen chloride. After redistillation of the substance, which was washed with alkali and water, and dried, 138.7 g (80.5% of the theoretical amount) of a light-yellow, thick oil with b.p. 181-183° at 4 mm was obtained; d_4^{15} 1.1761; n_D^{15} 1.5740.

0.1337 g substance: 0.0718 g AgCl. 0.1237 g substance: 0.0655 g AgCl. Found %: Cl 13.28, 13.30. $C_{15}H_{17}O_2Cl$. Calculated %: Cl 13.42.

After a two months' standing with a solution of semicarbazide, the substance thickened considerably, but a crystalline semicarbazone could not be isolated from it.

3-Keto-6-methoxy-1,2,3,9,10,10a-hexahydrophenanthrene (II. R = 6-CH_3O)

60 ml of sulfuric acid (d 1.74) was added in small portions with ice cooling to 45 g of ketone (IX). The mixture was left to stand overnight at room temperature. After 24 hours, the dark green solution was poured on ice, the precipitated product was rubbed with a glass rod and crystallized completely. The substance was filtered, washed with alkali and water, and dried. After recrystallization from alcohol (boiling with carbon), colorless

prisms with m.p. 111-112° were obtained. Yield, 24.7 g (63.67% of the theoretical amount).

0.1097 g substance: 0.3176 g CO_2; 0.0702 g H_2O. 0.1108 g substance: 0.3194 g CO_2; 0.0718 g H_2O. 0.2179 g substance: 0.2223 g AgI. 0.2094 g substance: 0.2155 g AgI. Found %: C 78.95, 78.61; H 7.11, 7.27; CH_3O-group 13.44, 13.60. $C_{14}H_{13}O(OCH_3)$. Calculated %: C 78.94; H 7.02; CH_3O-group 13.59.

The 2,4-dinitrophenylhydrazone, cinnabar colored, recrystallized from a mixture of chloroform and alcohol had a m.p. 233-234°.

0.1008 g substance: 19.6 ml N_2 (21°, 676 mm). Found %: N 13.95. $C_{21}H_{20}O_5N_4$. Calculated %: N 13.72.

3-Hydroxy-6-methoxyphenanthrene (X)

A mixture of 3 g of the ketone (II. R = 6-CH_3O) and 0.9 g sulfur was heated at 185-195° for $\frac{1}{2}$ hour until the evolution of hydrogen sulfide stopped. The viscous product which formed, dissolved almost completely upon rubbing with an excess amount of warm 10% sodium hydroxide solution. The solution was filtered from the small amount of the insoluble oily residue. Upon the acidification of the filtrate, the acidic dehydrogenation product separated in the form of an emulsion which soon formed flocculant crystals. After three recrystallizations from alcohol (boiling with carbon), 1.5 g (50.9% of the theoretical amount) of colorless thin crystals with m.p. 125° was obtained.

0.1018 g substance: 0.3012 g CO_2; 0.0526 g H_2O. 0.1014 g substance: 0.2994 g CO_2; 0.0520 g H_2O. Found %: C 80.69, 80.52; H 5.73, 5.69. $C_{15}H_{12}O_2$. Calculated %: C 80.36; H 5.35.

The red picrate, recrystallized from alcohol, melted at 165-166°.

0.1007 g substance: 9.2 ml N_2 (29°, 676 mm). 0.1007 g substance: 9.5 ml N_2 (29°, 674 mm). Found %: N 9.20, 9.47. $C_{21}H_{15}O_9N_3$. Calculated %: N 9.27.

3,6-Dimethoxyphenanthrene (XI)

1 g of dimethyl sulfate was added dropwise with stirring to a solution of 0.7 g of 3-hydroxy-6-methoxyphenanthrene in 25 ml of a 2% sodium hydroxide solution heated on the water bath. The mixture was heated for 15 minutes, 20 ml of a 4% sodium hydroxide solution added, and the heating continued for 15 minutes more. After cooling, the oily product was dissolved in ether, the ether solution washed with water, and dried with sodium sulfate. Upon the removal of the ether, needle-like crystals which melted at 104-105° after recrystallization from alcohol were obtained (3,6-dimethoxyphenanthrene [13]).

SUMMARY

1. α-(3-Chlorocrotyl)-γ-phenylbutyric acids containing a methoxyl group in the meta and para position of the aromatic ring were synthesized, and the products of the reaction of these acids with sulfuric acid were investigated.

2. It was shown for the example of α-(3-chlorocrotyl)-γ-(m-anisyl)butyric acid that the meta methoxyl group did not prevent the intramolecular acylation from occurring in the para position in relation to this group. The yield of the cyclization product was somewhat lower than those found for unsubstituted α-(3-chlorocrotyl)-γ-phenylbutyric acid and its aromatic methyl homologs, which, evidently, is explained by the favorable effect of the methoxyl group on the sulfonation of the starting acid.

3. Only traces of 3-keto-6-methoxyhexahydrophenanthrene, the product of the sulfuric acid hydrolysis and double cyclization of the latter, were formed by the action of sulfuric acid on α-(3-chlorocrotyl)-γ-(p-anisyl)butyric acid, which is explained by the effect of the para methoxyl group favoring the sulfonation of the starting acid and hindering the intramolecular acylation occurring in the meta position relative to this group. A satisfactory yield of 3-keto-6-methoxyhexahydrophenanthrene could only by achieved by a different method based on the separate cyclization of rings B and C.

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INVESTIGATIONS OF ALKANE SULFONIC ACIDS

IX. SYNTHESIS AND PROPERTIES OF ARYLAMIDES OF PHENYLMETHANESULFONIC ACIDS

A. G. Kostsova

A series of arylamides of phenylmethanesulfonic acid are reported in the present communication. The arylamides of methane and chloromethanesulfonic acids were reported in detail in the previous communications [1]. Reactions of phenylmethanesulfonyl chloride with aniline, o,p-toluidine, p-anisidine, p-phenetidine, and α-aminopyridine were conducted. It was found that phenylmethanesulfonyl chloride showed a sufficiently great reactivity: it reacts with the above amines under various conditions although somewhat more slowly than the alkanesulfonyl chlorides, which possess very high reactivity.

The anilide, o,p-toluidide, p-anisidide, p-phenetidide, and α-aminopyridide obtained are colorless, crystalline substances readily soluble in ether, alcohol, benzene, difficultly in water, dissolve in alkalies, and separate from the alkaline solutions upon acidification; they are sufficiently stable to hydrolysis, i.e., they show a great resemblance in properties to the aryl amides of alkane sulfonic acids.

The general equation for the reaction is the following:

$$C_6H_5CH_2SO_2Cl + 2NH_2Ar \longrightarrow C_6H_5CH_2SO_2NHAr + ArNH_2 \cdot HCl.$$

EXPERIMENTAL*

The following of the series of experiments conducted are given below: the starting phenylmethanesulfonyl chloride was prepared by the chlorination of phenylmethyl thiocyanate. An energetic stream of chlorine was passed for 1.5 hours at room temperature (18-20°) into a suspension of 4 g of freshly prepared phenylmethyl thiocyanate (m.p. 41°) in 30 ml of water. The temperature of the mixture rose to 50° and once more fell to 20-25°. The sulfonyl chloride accumulated on the bottom of the reaction vessel in the form of a dense yellow oil. At the end of the reaction, the mixture was cooled. The oily sulfonyl chloride gradually crystallized. The residue was filtered, washed several times with water, 5% sodium carbonate solution, once more with water, and then dried. Yield 1.25 g or 25% of the theoretical. A more prolonged chlorination at lower temperatures led to an insignificant yield of the sulfonyl chloride. Phenylmethanesulfonyl chloride, white crystals with m.p. 94°, was soluble in ether, benzene, acetone, and insoluble in water; it has an irritating action on skin.

1. Reaction of phenylmethanesulfonyl chloride with aniline. The procedure for conducting the reaction of phenylmethanesulfonyl chloride with aniline, as well as the isolation and purification of the reaction product, is reported in great detail; all of the subsequent experiments were conducted in an analogous manner; for this reason reports of subsequent experiments are omitted. 1.5 g of phenylmethanesulfonyl chloride was dissolved in 30 ml of absolute ether. 1.47 g of aniline was added to the solution in small portions. The solution clouded, and after 30-40 minutes aniline hydrochloride precipitated. The salt was filtered after 3-4 hours and was not investigated further. The ethereal filtrate was evaporated. The residue was treated with dilute alkali, the impurities insoluble in alkali were filtered, and the reaction product, phenylmethanesulfoanilide, was precipitated with dilute sulfuric acid. It was recrystallized from alcohol and water; m.p. 109°. Yield 0.63 g or 35% of the theoretical. A reaction in ether with heating on the water bath at 50° with reflux led to the same results. A reaction in absolute benzene with heating at 90° gave a yield of 70% of the theoretical of the product.

0.0389 g substance: 1.58 ml 0.1 N H_2SO_4. 0.1508 g substance: 0.1408 g $BaSO_4$. Found %: N 5.69; S 12.82. $C_{13}H_{13}O_2NS$. Calculated %: N 5.66; S 12.95.

2. Reaction of phenylmethanesulfonyl chloride with o-toluidine. 2 g of the chloride, 80 ml of absolute ether, and 2.2 g of o-toluidine were used. By dissolving the crude reaction product in alkali and by subsequently precipitating it with acid, it was isolated in the form of a yellow oil which crystallized only upon strong

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* N. P. Venevitinova and M. A. Gorshkova participated in the experimental work.

cooling. The crystals were greasy to touch. M.p. 65°. Yield 2.1 g or 78% of the theoretical. The reaction in absolute ether at room temperature lowered the yield to 55-56%; in benzene with heating the yield was 74-85%, at room temperature, 48-49% of the theoretical.

0.1018 g substance: 3.84 ml 0.1 N H_2SO_4. 0.1012 g substance: 0.0905 g $BaSO_4$. Found %: N 5.28; S 12.20. $C_{14}H_{15}O_2NS$. Calculated %: N 5.34; S 12.26.

3. Reaction of phenylmethanesulfonyl chloride with p-toluidine. The reaction was conducted with the same quantities of starting materials as in the previous experiment. Phenylmethanesulfo-p-toluidide was a white finely crystalline substance. M.p. 108°. Yield 1.5 g or 69-70% of the theoretical. The reaction is ether at room temperature gave a yield of 46% of the product, in benzene upon heating, 60%, at room temperature, 41-42% of the theoretical.

0.1020 g substance: 3.85 ml 0.1 N H_2SO_4. 0.1015 g substance: 0.0911 g $BaSO_4$. Found %: N 5.28; S 12.30. $C_{14}H_{15}O_2NS$. Calculated %: N 5.34; S 12.26.

4. Reaction of phenylmethanesulfonyl chloride with p-anisidine. 1.7 g of phenylmethanesulfonyl chloride, 2.1 g of p-anisidine, and 50 ml of absolute ether were used. Phenylmethylsulfo-p-anisidide was a white crystalline substance bitter to the taste. M.p. 101°. The yield was 1.1 g or 46% of the theoretical. The reaction in ether without heating gave a yield of 43%, in benzene upon heating 64-65% of the theoretical.

0.0380 g substance: 1.469 ml 0.1 N H_2SO_4. 0.1037 g substance: 0.0889 g $BaSO_4$. Found %: N 5.40; S 11.75. $C_{14}H_{15}O_3NS$. Calculated %: N 5.05; S 11.55.

5. Reaction of phenylmethanesulfonyl chloride with p-phenetidine. 2 g of phenylmethanesulfonyl chloride, 2.8 g of p-phenetidine, and 90 ml of absolute ether were used. Phenylmethanesulfo-p-phenetidide was obtained in the form of needles; m.p. 110°. Yield 1.9 g or 87% of the theoretical. The reaction in ether without heating gave a yield of 55.6%, in benzene with heating 93%; without heating 87% of the theoretical.

0.1022 g substance: 3.47 ml 0.1 N H_2SO_4. 0.0904 g substance: 0.0720 g $BaSO_4$. Found %: N 4.75; S 10.92. $C_{15}H_{17}O_3NS$. Calculated %: N 4.79; S 10.99.

6. Reaction of phenylmethanesulfonyl chloride with α-aminopyridine. 2 g of phenylmethanesulfonyl chloride and 1.85 g of α-aminopyridine were dissolved in 20 ml of benzene. The mixture was shaken for 20-30 minutes. A clouding and a slight amount of heating occurred (23-25°). Soon a yellow oil formed on the bottom of the reaction flask. After standing for some time, the oil was separated and vacuum distilled; a small amount of unreacted α-aminopyridine was removed; the remaining part of the oil decomposed upon distillation. The benzene solution, after the removal of the oil, was evaporated in a porcelain dish. With the evaporation, light yellow scaly crystals of phenylmethanesulfo-α-aminopyridide precipitated on the walls of the dish. They became colorless upon recrystallization from water. Yield, 68% of the theoretical. M.p. 143°. Upon treatment with 5% alkali followed by acidification with sulfuric acid, the product precipitated only when there was a strictly neutral reaction; with an excess of acid, it dissolved, forming apparently, a water-soluble salt because of the tertiary nitrogen atom of the pyridine residue. Upon conducting the reaction in acetone at room temperature, the yield of the product was 1.97 g or 75-76% of the theoretical; in benzene and in acetone with heating, the crystalline product was not formed at all, or an oil separated from which definite compounds could not be isolated.

0.2331 g substance: 17.967 ml 0.1 N H_2SO_4. 0.1836 g substance: 0.1690 g $BaSO_4$. Found %: N 10.79; S 12.62. $C_{12}H_{12}O_2N_2S$. Calculated %: N 11.29; S 12.90.

SUMMARY

1. The reactions of phenylmethanesulfonyl chloride with aniline, o- and p-toluidine, p-anisidine, p-phenetidine, α-aminopyridine were studied under various conditions.

2. The anilide, o- and p-toluidide, p-anisidide, p-phenetidide, and α-aminopyridide of phenylmethanesulfonic acid were prepared and characterized for the first time.

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Voronezh State University

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INVESTIGATIONS OF IMIDAZOLE DERIVATIVES

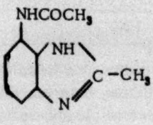
VIII. STUDY OF NITRATION AND AZOCOUPLING REACTIONS OF 4-AMINOBENZIMIDAZOLE [1]

L. S. Efros

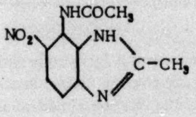
The aim of the present investigation was to study the effect of amino group in position 4 of benzimidazole on the benzene ring of these compounds during nitration and azo coupling reactions.

The start of the investigation was a study of the nitration of 4-acetylamino-2-methylbenzimidazole (I), which proceeded very smoothly in concentrated sulfuric acid.

The reaction product could be separated by means of crystallization from alcohol into two isomeric substances (II and III) which were obtained in an approximately 1:2 ratio.



(I)



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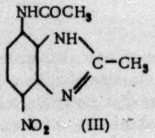
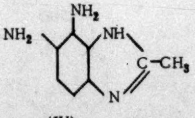


(III)

Both of these substances hydrolyzed readily upon boiling in dilute hydrochloric acid to form the free amines which were capable of diazotization, and subsequently, of participating in coupling reactions.

The amine from product (II), obtained in lower yield, was in the form of yellow platelets, the amine isomeric with it from product (III), light yellow needles, In order to prove the structure both amines were reduced with tin and hydrochloric acid into the unstable diamines (IV) and (V).



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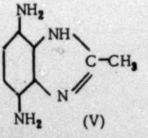
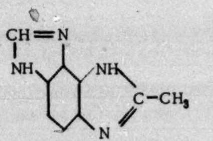


(V)

o-Diamine (IV) without further purification, was treated with anhydrous formic acid; another imidazole ring formed and a stable unhydrolyzable methyl derivative of diimidazolo-1,2,3,4- benzene (VI) unhydrolyzed upon treatment with acids, crystallizing from water in the form of white needles was obtained.

Analogously, upon treating diamine (IV) with glacial acetic acid in a sealed tube at 180°, dimethyldiimidazolo-1,2,3,4-benzene (VII) was obtained.



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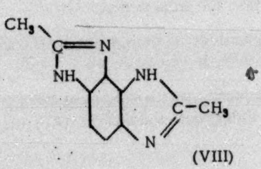


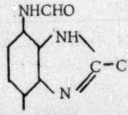
(VIII)

This compound (VII) was previously reported by Nietzki [2] who obtained it during the process of proving the structure of dinitrosoresorcinol.

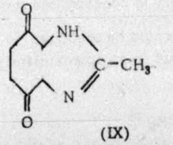
However, according to Nietzki's data, the melting point of compound (VII) was lower than that for the product obtained by more than 100°. In view of this, the reported synthesis was repeated, and a substance was obtained in a very low yield which melted as the above and gave no depression upon mixing after thorough purification.

As for the p-diamine (V), it gave a stable and poorly-soluble salt with sulfuric acid, in which form it was possible to purify and analyze it. In contrast to diamine (IV), this compound only formed the diformyl derivative (VIII) upon boiling with formic acid, which was readily cleaved upon heating with mineral acids to form the unstable diamine.

By careful oxidation of the p-diamine (V) with chromic acid, a new interesting derivative of benzoquinone with an imidazole ring (IX) was obtained.



(VIII)



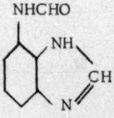
(IX)

This compound, crystallizing in the form of bright orange-yellow needles, was found to be quite unstable. It dissolved readily in mineral acids with a light yellow color. In alkali solution, however, this compound decomposed very rapidly; the bright color of the solution almost at once became cloudy, and the starting substance could not be isolated from it. A noticeable decomposition of the product occurred even upon heating with water.

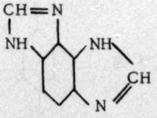
The nitration of 4-formaminobenzimidazole (X) was studied analogously.

In this case, the mixture of ortho and para aminonitro-derivatives could not be successfully separated, which was obtained by nitration; for this reason, the mixture of these substances, after treatment with hydrochloric acid, was reduced with tin, and without any further purification, treated with anhydrous formic acid. The reaction product was separated into two substances by recrystallization from water; one of these, obtained in smaller amount, was found to be stable to hydrochloric acid treatment, and had the structure of diimidazolo-1,2,3,4-benzene (XI).

The other product, readily hydrolyzable by boiling with hydrochloric acid, is the diformyl derivative of p-diamine (XII).



(X)



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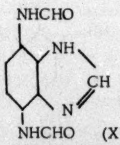
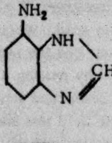


(XII)

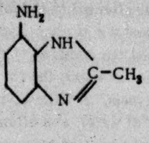
Upon treatment of the reduction products of this mixture of nitro compounds with acetic acid in a sealed tube at 180°, methyldiimidazolo-1,2,3,4-benzene was isolated which was found to be identical with the previously reported compound (VI) obtained by the condensation of o-diamine (IV) with formic acid. In this way, it was proved that, during nitration of acyl derivatives of 4-aminobenzimidazole, and 4-amino-2-methylbenzimidazole, a mixture of the ortho and para isomers of the corresponding aminonitro derivatives was obtained. More of the para isomer is contained in this mixture than the ortho isomer.

Later, the coupling reaction of 4-aminobenzimidazole (XIII) and 4-amino-2-methylbenzimidazole (XIV) with diazo compounds was studied.

As expected, it was found that the substances readily participated in diazo coupling reactions. Dyes, obtained from them, upon coupling with diazotized aniline, (XV) and (XVI), were purified and analyzed.



(XIII)



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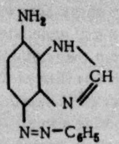
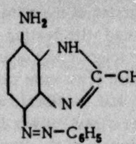


(XV)



(XVI)

The above structures for these substances were proved by reduction and subsequent treatment with anhydrous formic acid. The diformyl derivatives of 4,7-diaminobenzimidazole obtained were found to be identical with the previously reported compounds (VIII) and (XII) synthesized from 4,7-diaminonitrobenzimidazoles.

Therefore, the amino group found in position 4 of benzimidazole, has a large activating effect on the benzene ring of these compounds and made the coupling reaction with diazo compounds possible. The latter reaction goes exclusively para to the amino group (position 7), whereas during nitration, although in smaller yield, the ortho isomer is also obtained. The specific activity of positions 5 and 6 of benzimidazole is not affected.

EXPERIMENTAL

I. Nitration of Acyl Derivatives of 4-Aminobenzimidazole *

1. Nitration of 4-Acetylamino-2-methylbenzimidazole.

9 g of the product was dissolved in 60 ml of conc. sulfuric acid, keeping the temperature below 15-20°. Then, a nitrating mixture of 4 ml nitric acid (d 1.5) and 8 ml of conc. sulfuric acid was added dropwise at this temperature with stirring without allowing an increase in temperature. 15 minutes after the addition, the mass was poured onto ice, and the solution was carefully neutralized with ammonia with the addition of ice (temperature not higher than 40-50°). The light yellow product which separated was filtered, washed with water until not acid, and dried. The product obtained was dissolved with heating in alcohol and the hot solution was separated from a small amount of alcohol-insoluble impurities. Upon cooling, 7-nitro-4-acetylamino-2-methylbenzimidazole crystallized from it in the form of light yellow shiny platelets. A small amount more of this product was isolated upon the evaporation of the alcoholic mother liquor to one third the volume. The total yield of this isomer was 3.2-3.8 g.

The residue remaining after complete removal of the alcohol from the mother liquor, was mainly the second isomer, 5-nitro-4-acetylamino-2-methylbenzimidazole, partly saponified. It was very soluble in alcohol and did not crystallize from it. This residue was heated for 15-20 minutes with 5-10 ml of 10% hydrochloric acid. After cooling, the amine hydrochloride slowly separated in the form of orange-yellow square or rhombic platelets. The yield of this product was 1.3-1.6 g.

The acetyl derivative of 7-nitro-4-amino-2-methylbenzimidazole was a light-yellow, shiny, platelet-like crystalline substance with m.p. 315-318° (with preliminary softening and darkening).

0.1320 g substance: 0.2477 g CO_2; 0.0495 g H_2O. 0.1040 and 0.1065 g substance: 21.7, 28.3 ml N_2 (22°, 754 mm). Found %: C 51.20; H 4.17; N 23.95, 24.05. $C_{10}H_{10}O_3N_4$. Calculated %: C 51.30; H 4.27; N 23.90.

7-Nitro-4-amino-2-methylbenzimidazole. For saponification, 0.5 g of the product was dissolved in 15 ml of 5% hydrochloric acid; the hydrochloride precipitated and was dissolved upon heating. Soon, however, long, light-yellow needles of 7-nitro-4-amino-2-methylbenzimidazole precipitated from the boiling solution. They were filtered and recrystallized from water containing hydrochloric acid.

0.1050 g substance: 0.0659 g AgCl. 0.1002 and 0.1005 g substance: 21.1 ml and 21.2 ml N_2 (22°, 762 mm).

Found %: N 24.5, 24.6; Cl 15.5. $C_8H_8O_2N_4 \cdot HCl$. Calculated %: N 24.5; Cl 15.5.

In order to convert to the base, the 7-nitro-4-amino-2-methylbenzimidazole salt was dissolved in water, carefully neutralized with ammonia, and recrystallized from water. Fine, light-yellow, shiny crystals with m.p. 291-293°.

0.1081 and 0.1098 g substance: 27.5 ml and 28.0 ml N_2 (22°, 760 mm). Found %: N 29.45, 29.5. $C_8H_8O_2N_4$. Calculated %: N 29.15.

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* For the synthesis of 4-acetylaminobenzimidazole, see the following communication (p. 995).

The reduction of the nitro group of this compound was effected in the following manner: 2 g of the hydrochloride was treated with heating with 5 g of granulated tin and 5 g of conc. hydrochloric acid. When the reaction was finished, the solution was poured from the residual tin, and the complex of the tin salt and the reduction product began to crystallize after some time. It was filtered, dissolved in water, the tin removed by passing a stream of hydrogen sulfide, and the filtrate evaporated in vacuum to dryness. A white crystalline compound was obtained which was very easily oxidized. It was dissolved in a small amount of water, and dilute sulfuric acid was added. A white needle like precipitate of the diamine sulfate formed which was purified by recrystallization from dilute hydrochloric acid using active carbon.

0.1173 and 1170 g substance: 0.1054 and 0.1050 g $BaSO_4$. Found %: H_2SO_4 37.8, 37.65. $C_8H_{10}N_4 \cdot H_2SO_4$. Calculated %: H_2SO_4 37.70.

For the preparation of methylimidazolobenzoquinone, 2 g of the diamine hydrochloride (obtained directly by the reduction of the nitro product) was dissolved in 20 ml of water, a small amount of dilute sulfuric acid and a solution of 2 g of chromic acid in water was added. The amine sulfate which precipitated upon the addition of the sulfuric acid, dissolved quite rapidly; the solution was heated up to a slight extent by the oxidation reaction occurring. After a half hour, sodium acetate was added to the solution until the absence of an acidic reaction to Congo; the yellow needles of the quinone which precipitated were filtered, and washed with water. The product was purified by 3 times dissolving the product in cold dilute hydrochloric acid and precipitating with sodium acetate followed by washing with water. Yield 0.9 g. The product decomposed over 360°; it did not melt.

The quinone was readily soluble in dilute mineral acids and alkalies with the formation of bright raspberry red solutions which, however, rapidly clouded because of the decomposition of the product. Upon heating with water, it also noticeably decomposed.

0.1409 and 0.1268 g substance: 0.3073 and 0.2770 g CO_2; 0.0493 and 0.0423 g H_2O. 0.1018 and 0.1030 g substance: 15 (18°, 762 mm) and 15.3 ml N_2 (20°, 758 mm).

Found %: C 59.40, 59.45; H 3.88, 3.71; N 17.30, 17.30. $C_8H_6O_2N_2$. Calculated %: C 59.27; H 3.71; N 17.30.

In order to prepare the diformyl derivative of 4,7-diamino-2-methylbenzimidazole, 2 g of the diamine hydrochloride, obtained by the reduction of the nitro product, was dissolved by heating in 10 ml of anhydrous formic acid and refluxed for 2 hours. The solution was evaporated almost to dryness on the water bath, neutralized with ammonia and after cooling, the precipitated diformyl derivative of 4,7-diamino-2-methylbenzimidazole was filtered. Yield 1.2 g. The product was recrystallized from water over active carbon. White thin needles with m.p. 268-270°, (with initial softening). The compound obtained was readily hydrolyzed by hydrochloric acid with heating. The solution obtained in this manner, after neutralization with ammonia, darkened very rapidly, then turned black, and nothing could be isolated from it but dark tarry flocs. Upon conducting the reaction with sulfuric acid, needles of the diamine sulfate reported above came out of the solution.

0.1210 g substance: 0.2440 g CO_2; 0.0500 g H_2O. 0.1168 and 0.1003 g substance: 26.2 and 22.3 ml N_2 (22°, 753 mm). Found %: C 54.90; H 4.59; N 25.7; 25.5. $C_{10}H_{10}N_4O_2$. Calculated %: C 54.95; H 4.58; N 25.7.

5-Nitro-4-amino-2-methylbenzimidazole. The hydrochloride crystallized from aqueous hydrochloric acid as bright yellow square or rhombic platelets. It was considerably more soluble in water than the salt of the second isomer. It did not have a definite melting point.

0.0980 and 0.0951 g substance: 21 and 20.5 ml N_2 (22°, 754 mm). 0.0672 g substance: 0.0420 g AgCl. Found %: N 24.5, 24.7; Cl 15.4. $C_8H_8O_2N_4 \cdot HCl$. Calculated %: N 24.5; Cl 15.3.

The base of the product was obtained by treating the salt with an ammonia solution and recrystallization from aqeuous alcohol. Yellow crystals with m.p. 300-302°.

0.0598 and 0.0734 g substance: 15.2 and 18.6 ml N_2 (22°, 760 mm). Found %: N 29.3, 29.3. $C_8H_8O_2N_4$. Calculated %: N 29.15.

The reduction of the product was effected, as in the previous case, with tin and hydrochloric acid. The yield from 2 g of the hydrochloride was 0.9-1.1 g of diamino-2-methylbenzimidazole hydrochloride. The product, without further purification, was dissolved in 10 ml of anhydrous formic acid and refluxed for 2 hours. The solution was evaporated almost to dryness on the water bath, dissolved in water, and the reaction product precipitated with ammonia. Yield 0.8–0.9 g. Methyl-1,2,3,4-diaminodiimidazolobenzene obtained in this manner, was recrystallized from water; long white needles with m.p. 312-314°. It was readily soluble in dilute hydrochloric acid, it was not decomposed by prolonged boiling, and was precipitated from solution by the addition of ammonia;

0.0910 g substance: 0.2076 g CO_2; 0.0403 g H_2O. 0.1032 and 0.1035 g substance: 29.0 and 29.0 ml N_2 (22°, 762 mm). Found %: C 62.20; H 4.00; N 32.70, 32.65. $C_9H_8N_4$. Calculated %: C 62.80; H 4.65; N 32.55.

1 g of 4,5-diamino-2-methylbenzimidazole hydrochloride was heated in a sealed tube with 7 ml glacial acetic acid at 180° for 1 hour. The liquid was evaporated to dryness, the residue dissolved in water, and dimethyl-1,2,3,4-diimidazolobenzene precipitated with ammonia. Yield 0.6 g. The product was purified by recrystallization from water; white needles with m.p. 292-294°. It was readily soluble in alcohol, poorly in water (about 1 g of the product dissolved in 100 ml of boiling water); it was readily soluble in dilute hydrochloric acid and unchanged upon continued heating with it.

0.1002 and 0.0991 g substance: 0.2350 and 0.2331 g CO_2; 0.0483 and 0.0479 g H_2O. 0.1161 and 0.1101 g substance: 30.4 (22°, 754 mm) and 28.7 ml N_2 (20°, 754 mm). Found %: C 63.96, 64.20; H 5.58, 5.37; N 30.1, 30.2. $C_{10}H_{10}N_4$. Calculated %: C 64.5; H 5.4; N 30.1.

2. Nitration of 4-Formaminobenzimidazole. 11 g of formaminobenzimidazole was carefully dissolved in 40 ml of conc. sulfuric acid, and a nitrating mixture of 3.5 ml of nitric acid (d 1.5) and 1.5 ml of sulfuric acid was added dropwise at 10-15° to the solution. The reaction mass was poured onto ice and carefully neutralized with ammonia, not allowing the solution to heat up. The yellow nitration product which separated was filtered and washed with water. Yield 9 g. The product, without further purification, was reduced by 15 g of tin and 20 ml of conc. hydrochloric acid. The complex which separated was dissolved after filtration, the tin precipitated with hydrogen sulfide, and the solution obtained evaporated to dryness in vacuum. The residue was boiled with 30 ml of anhydrous formic acid for 2 hours, the formic acid was evaporated, the residue dissolved in water, and the reaction product precipitated with ammonia. The reaction product was subjected to fractional crystallization from water. The more difficultly soluble 1,2,3,4-diimidazolobenzene, obtained in a yield of 2.5-3.0 g, crystallized. 1,2,3,4-Diimidazolobenzene was boiled with 5% HCl, precipitated from ammonia solution, and recrystallized from water with activated carbon for complete purification from the second product. Yield 0.5-0.9 g; m.p. 288-296°.

0.1055 g substance: 0.2360 g CO_2; 0.0361 g H_2O. 0.1032 g and 0.1036 g substance: 31.8 ml and 31.8 ml N_2 (21°, 754 mm). Found %: C 60.90; H 3.80; N 35.50, 35.50. $C_8H_6N_4$. Calculated %: C 60.75; H 3.80; N 35.45.

4,7-Diformaminobenzimidazole was a long,needle-like crystalline substance readily soluble in dilute hydrochloric acid. M.p. 292-293°.

0.1354 and 0.1215 g substance: 0.2602 and 0.2360 g CO_2; 0.0500 and 0.0478 g H_2O. 0.1120 and 0.1430 g substance: 27 (22°, 754 mm) and 34.4 ml N_2 (22°, 758 mm). Found %: C 52.30, 52.95; H 4.18, 3.93; N 27.70, 27.70. $C_9H_8O_2N_4$. Calculated %: C 52.90; H 3.92; N 27.45.

3 g of the above product of the reduction of the nitro compound was heated with 15 ml of glacial acetic acid at 180° in a sealed tube for 1 hour. The condensation product, precipitated by neutralization with ammonia, was treated with hydrochloric acid with heating to remove the acetyl derivative, precipitated with ammonia, and purified by recrystallization from water with active carbon. A yield of 0.3 g of methyl-1,2,3,4-diimidazolobenzene was obtained, which was identical in properties with that previously obtained.

II. Coupling of 4-Aminobenzimidazole and Its 2-Methyl Derivative with Diazotized Aniline

8 g 4-aminobenzimidazole dihydrochloride was dissolved in 50 ml of water; diazotized aniline and sodium acetate were added to the solution until the absence of an acidic reaction on Congo. A coupling occurred which resulted in the solution turning orange, and upon standing, an azo dye began to precipitate. After an hour, it was filtered, washed with a small amount of water, pressed, and dried. Yield 12 g.

The dye, in the form of the monohydrochloride, crystallized from water in the form of red needles not having a definite melting point. Aqueous solutions were colored red-orange; upon the addition of hydrochloric acid, they became violet red; upon the addition of ammonia, the dye base precipitated in the form of a tar.

0.1023 and 0.1030 g substance: 23.0 and 23.1 ml N_2 (22°, 754 mm). 0.0922 and 0.0957 g substance: 0.0482 and 0.0503 g AgCl. Found %: N 25.80, 25.80; Cl 12.92, 13.02. $C_{13}H_{10}N_5 \cdot HCl$. Calculated %: N 25.70; Cl 13.03.

The coupling of diazotized aniline with 4-amino-2-methylbenzimidazole was effected in an analogous manner. 7 g of the dye, in the form of the monohydrochloride, was obtained from 6 g of the amine dihydrochloride. Its properties were similar to those of the one previously described.

0.1183 and 0.1119 g substance: 25.6 and 23.7 ml N_2 (22°, 754 mm). 0.1003 g substance: 0.0497 g AgCl. Found %: N 24.80, 24.35; Cl 12.50. $C_{14}H_{12}N_5 \cdot HCl$. Calculated %: N 24.45; Cl 12.37.

In order to prove the structures, both dyes were reduced with tin and hydrochloric acid. The complex which precipitated was dissolved in water, and the tin was removed with hydrogen sulfide. The filtrate was evaporated to dryness in vacuum, and the solid white residue of the amine salts obtained was boiled for 2 hours with anhydrous formic acid. The formic acid solution obtained was evaporated to dryness on the water bath, the residue was dissolved in water, and the reaction product, precipitated by the action of ammonia, was purified by recrystallization from water with activated carbon. Products were obtained which were found to be identical with the previously reported diformyl derivatives of 4,7-diaminobenzimidazole and 2-methyl-4,7-diaminobenzimidazole.

SUMMARY

The amino group found in position 4 of benzimidazole has a great activating effect on the benzene ring of these compounds. Because of this effect, 4-aminobenzimidazoles readily participate in azo coupling reactions to form p-amino azo dyes exclusively. Upon the nitration of acyl derivatives of 4-aminobenzimidazole, mixtures of ortho and para nitro derivatives containing a larger amount of the para isomer were obtained.

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* See Consultants Bureau English Translation, p. 881.

** See Consultants Bureau English Translation, p. 1063

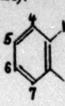
INVESTIGATIONS OF IMIDAZOLE DERIVATIVES

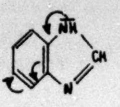
IX. SYNTHESIS OF 4-AMINOBENZIMIDAZOLE AND COMPARISON OF ITS CHEMICAL PROPERTIES WITH THOSE OF 5-AMINOBENZIMIDAZOLE [1]

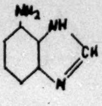
L. S. Efros

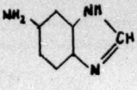
In the previous investigations [2,3], it was shown that the imidazole group causes a considerable destruction of symmetry in relation to the benzene ring in the benzimidazole molecule, wherein the double bond character of the 4-5 and 6-7 carbon atoms increases while the 5-6 carbon atom bond resembles the regular ones. With such a distribution of bonds, benzimidazole (I a) must resemble naphthalene [4] in its chemical properties; however, in contrast to the latter, positions 5 and 6, not 4 and 7, possess greater reactivity in the compounds examined, which correspond to the less active position in naphthalene. The reason for the above behavior of benzimidazole is the direction of the effect of the nitrogen atoms of the heterocycle, which is transferred along a chain of conjugated double bonds. The reactive ends of these chains are found in positions 5 and 6 because there is a certain amount of disruption in conjugation between these positions (I b).

From this point of view, it seemed interesting to compare the chemical properties of 4-amino- and 5-aminobenzimidazole (II and III):


Ia


Ib


II


III

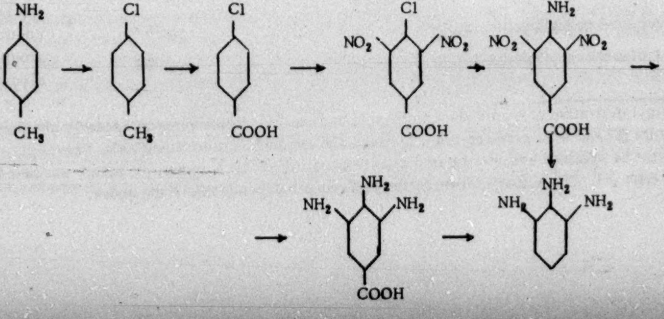
It would be expected that the amino group in the unreactive benzimidazole position 4 would not noticeably affect the basicity of the compound, while the effect of the amino group in position 5 must be considerable.

It seemed of interest to study the effect of the amino groups of these compounds on the benzene ring. This study could determine whether or not the above-mentioned interruption in the conjugation between carbon atoms 5 and 6 in the benzimidazole was retained with the presence of an amino group in position 4; if it was retained, then the substitution reactions with compounds of type II must occur preferentially at the o-position to the amino group (position 5); if it was not retained, at the p-position (position 7).

The preparation of 5-aminobenzimidazole derivatives did not entail any sort of difficulty. They were synthesized by the reduction of the corresponding nitro derivatives obtained by the nitration of the benzimidazoles.

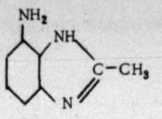
As for the 4-aminobenzimidazole derivatives, it was necessary to synthesize the ordinary triaminobenzene. The formation of the latter by the decarboxylation of 3,4,5-triaminobenzoic acid was reported by Salkowsky [5].

The synthesis of the ordinary triaminobenzene was accomplished by the following scheme:

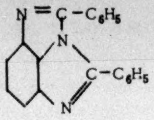


The overall yield of triamino benzene was 20-2 % of the theoretical. By heating the product with anhydrous formic acid, the formyl derivative of 4-aminobenzimidazole was obtained, from which the free amine (II) was formed by saponification with hydrochloric acid.*

By heating triaminobenzene with acetic acid and subsequent saponification, the previously reported by Salkowsky, 4-amino-2-methylbenzimidazole (IV) and its acetyl derivative were obtained.

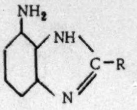


(IV)



(V)

Attempts to obtain analogous products by the fusion of ordinary triaminobenzene with benzoic acid and phenylacetic acid were unsuccessful. Substances were obtained in reactions under these conditions, which did not contain amino groups, and did not cleave even upon prolonged boiling with hydrochloric acid. It is possible that these compounds were products of a further cyclization of the acylaminobenzimidazole of structure (V), which Auwers and Frese [9] tried unsuccessfully to prepare. For this reason, the 4-amino-2-phenylbenzimiadazoles and 4-amino-2-benzylbenzimidazoles which were of further interest and unreported in the literature, were obtained by the condensation of triaminobenzene and these acids in a hydrochloric medium in sealed tubes under pressure [10].



(VI)

$R = C_6H_5$ and

$R = CH_2{-}C_6H_5$

The 4-aminobenzimidazoles, as well as the analogous 5-amino derivatives obtained, were titrated potentiometrically. The basicity constants found are given in the Table.

Comparison of the Effect of the Amino Group on the Basicity of the Benzimidazole Ring

Expt. No.	Product studied	Basicity constant of the benzimidazole ring	Basicity constant of the amino group
1	Benzimidazole	$10^{-8.6}$	–
2	4-Aminobenzimidazole	$10^{-8.7}$	$10^{-12.5}$
3	5-Aminobenzimidazole	$10^{-7.4}$	$10^{-10.7}$
4	2-Methylbenzimidazole	$10^{-8.3}$	–
5	4-Amino-2-methylbenzimidazole	$10^{-8.1}$	$10^{-12.3}$
6	5-Amino-2-methylbenzimidazole	$10^{-7.1}$	$10^{-11.2}$
7	2-Benzylbenzimidazole	$10^{-8.9}$	–
8	4-Amino-2-benzylbenzimidazole	$10^{-8.6}$	$10^{-11.9}$
9	5-Amino-2-benzylbenzimidazole	$10^{-7.6}$	$10^{-10.7}$

As it is apparent from the Table, and as was expected, amino groups found in position 4, do not essentially effect the basicity constants of the benzimidazole derivative, while those in position 5, increase this constant by about 20 times. This means that the electron pair of the amino in position 5 is shifted considerably toward the imidazole ring, in contrast to the amino group in position 4, the electrons of which are not shifted in this direction. A logical conclusion from the above (if approximately equal effects of these amino groups on the benzene ring are assumed) must be that the amino group found in position 4 is more basic than that in position 5. This fact which initially seemed unexpected, meant that the above assumption of the approximate equality of the effects of these amino groups is untrue, and actually, the amino group in position 4 shows a much greater effect on the benzene ring than that in position 5. This conclusion was completely confirmed by the study of the nitration and azo coupling of reactions of derivatives of 4- and 5-aminobenzimidazole.

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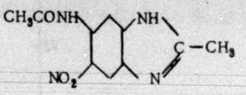
* The formyl derivative of 4-aminobenzimidazole and the free amine werevery recently obtained and reported in the literature [6] and were patented in Switzerland and England as pharmaceuticals. Previously, Wooley [8] believed that he obtained and investigated 4-aminobenzimidazole; however, his belief was based on a major chemical error [6]. The author's investigation proceeded independently of the above.

The nitration of 5-acetylamino-2-methylbenzimidazole is reported in the literature [11]; it was shown that the nitro group enters exclusively into position 6 to form product (VII):



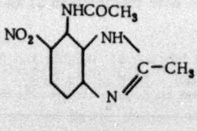
(VII)

Not even traces of any other isomeric products are to be found. Previously [2], examining this reaction, it was shown on the basis of a series of facts, that its direction is not determined by the effect of the amino group which must direct mainly to position 4, but of the specifically greater reactivity of positions 5 and 6 in the benzimidazole molecule. This view found experimental verification in experiments on the coupling of 5-amino-benzimidazole and 5-amino-2-methylbenzimidazole with diazo compounds.

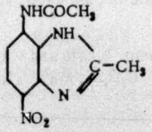
It was found that these substances were unable to couple, and even with the most active diazo compounds, only diazonium derivatives were formed, which were cleaved by mineral acids into the starting products.

Therefore, the amino group in position 5 of the benzimidazole ring is found in conjugation with the imidazole group which has only a slight effect on the benzene ring, insufficient to enable these compounds to participate in coupling reactions.

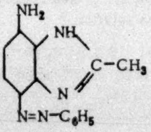
The nitration of 4-formaminobenzimidazole and 4-acetyl amino-2-methylbenzimidazole, reported in the previous communication [1], occurs very smoothly in concentrated sulfuric acid. As it was accurately shown, two isomeric mononitro compounds were formed in both cases, ortho (VIII) and para (IX), approximately in a ratio of 1:2.



(VIII)



(IX)



(X)

It was found that 4-aminobenzimidazole and its derivatives readily participated in azocoupling. The diazo group entered exclusively in the p-position to the amino group (position 7) to form p-amino dyes (X).

Therefore, the data given, confirming the conclusion given on the basis of the results of potentiometric titration of the benzimidazole derivatives, show that an amino group in position 4 of benzimidazole has a great effect on the benzene ring of this compound; it activates it and even makes the azo coupling reaction possible. The substituent group enters mainly into the p-position to the amino group (position 7) which indicates the absence of interference in the conjugation between carbon atoms 5 and 6 in the 4-aminobenzimidazole derivative molecules. In spite of this, for some unexplained reason, the amino group in position 4 almost does not interact with the imidazole ring. All of the facts jointly create the impression that two systems of conjugation with little mutual interaction are present in molecules of 4-aminobenzimidazole derivatives; an aminobutadiene and an imidazole.

EXPERIMENTAL

4-Aminobenzimidazole

10 g of triaminobenzene was heated for an hour to reflux in a flask with 40 ml of 97% of formic acid. The

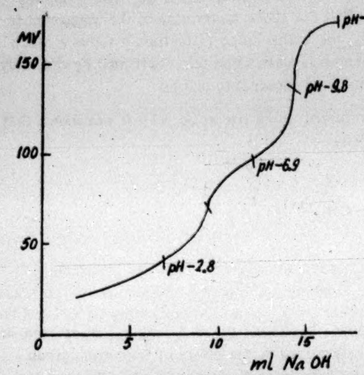


Fig. 1. Titration of 5-amino-2-methylbenzimidazole

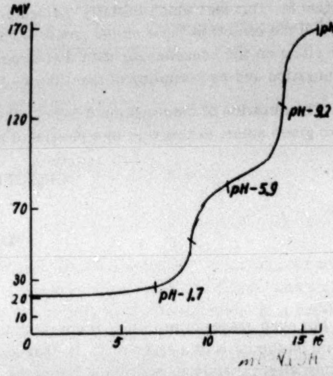


Fig. 2. Titration of 4-amino-2-methylbenzimidazole

tea-colored solution obtained was evaporated almost to dryness on the water bath, dissolved with heating in 50 ml of water, neutralized with ammonia, and after cooling, the almost white precipitate was filtered. The product was obtained chemically pure after one recrystallization from water with activated carbon. The yield of the formyl derivative of 4-aminobenzimidazole was 13 g, m.p. 172-174°.

0.1366 and 0.1422 g substance: 31.0 (22°, 762 mm) and 32.3 ml (23°, 760 mm) N_2. Found %: N 26.3, 26.15. $C_8H_7ON_3$. Calculated %: N 26.08.

The saponification of the formyl derivative was effected by a 15 minute heating with 10-15% hydrochloric acid. The solution obtained was evaporated on the water bath until the start of crystallization, and after cooling, the precipitated 4-aminobenzimidazole hydrochloride was filtered. Dense, very slightly rose needles of the product were isolated in almost theoretical yield, and only traces of it remained in the mother liquor. The product did not have a sharp melting point. It was readily soluble in cold water, and free base precipitated as an oil by the addition of ammonia to the solution.

0.1020 g substance: 18.2 ml N_2 (22°, 754 mm). 0.1472 and 0.1513 g substance: 0.2062 and 0.2119 g AgCl. Found %: N 20.47; Cl 34.68, 34.64. $C_7H_7N_3 \cdot 2HCl$. Calculated : N 20.4; Cl 34.5.

4-Amino-2-methylbenzimidazole [5]

10 g of triaminobenzene was heated to reflux for 6-8 hours with 40 ml of glacial acetic acid. The almost black solution obtained was evaporated to dryness on the water bath, the residue dissolved in hot water, and precipitated with ammonia. After cooling, the product was filtered and recrystallized from water with active carbon. Yield 15 g. The product, the acetyl derivative of 4-amino-2-methylbenzimidazole, contained 2 molecules of crystallization water and melted widely at 93-100°.

The saponification of the acetyl derivative was effected in the same manner as in the previous case. The yield of the amine dihydrochloride was almost quantitative. The salt did not have a definite melting point, and was readily soluble in water; the free amine was obtained in the form of a tar by the action of ammonia.

4-Amino-2-phenylbenzimidazole

Experiments on the preparation of the above product by melting triaminobenzene with benzoic acid (1:2) at 180° led to the preparation of a substance not containing a free amino group and which was unchanged even after prolonged boiling with 15% hydrochloric acid. Evidently, triaminobenzene formed compound (V) containing 3 rings under these conditions, which was also confirmed by the results of elementary analysis.

0.1016, 0.1010 g substance: 12.9 ml N_2 (22°, 754 mm); 12.4 ml N_2 (20°, 754 mm). Found %: N 14.6, 14.2. $C_{20}H_{13}N_3$. Calculated %: N 14.2.

For this reason, 4-amino-2-phenylbenzimidazole was subsequently prepared by heating 2 g of triaminobenzene, 2 g of benzoic acid, and 5 ml of 15% hydrochloric acid to 180° in a sealed tube. The reaction mass was treated with ammonia, and the product which separated in the form of a tar, was removed and recrystallized from water with hydrochloric acid. The yield of the product, obtained in the form of colorless needles of the dihydrochloride, was 0.3 g. The salt did not have a sharp melting point.

The base, which crystallized from alcohol in the form of needles, melted sharply at 210-211°.

0.1010 g substance: 0.2772 g CO_2, 0.0482 g H_2O. Found %: C 74.7; H 5.3. $C_{13}H_{11}N_3$. Calculated %: C 74.6; H 5.27.

4-Amino-2-benzylbenzimidazole

4 g of triaminobenzene and 4 g of phenylacetic acid were heated with 10 ml of 10% hydrochloric acid in a sealed tube at 180° for 2 hours. The reaction mixture was treated with ammonia, and the product precipitated in the form of an oil which rapidly solidified. It was recrystallized from water containing hydrochloric acid, and colorless shiny needles of the dihydrochloride were obtained. Yield 3.9 g, m.p. 242-248°, which was not very sharp.

0.1100 g substance: 13.8 ml N_2 (24°, 758 mm). 0.1456 and 0.1460 g substance: 0.1414 and 0.1415 g AgCl. Found %: N 14.37; Cl 24.05, 24.05. $C_{14}H_{13}N_3 \cdot 2HCl$. Calculated %: N 14.20; Cl 24.00.

The hydrochloride of the product was converted into the base by the action of an ammonia solution. The product was recrystallized from aqueous alcohol, M.p. 152-154°.

0.1376 g substance: 0.3804 g CO_2; 0.0687 g H_2O. 0.1076 and 0.1115 g substance: 17.8 ml N_2 (22°, 750 mm) and 18.6 ml N_2 (24°, 758 mm). Found %: C 75.36; H 5.54; N 19.10, 19.10. $C_{14}H_{13}N_3$. Calculated %: C 75.25; H 5.83; N 18.85.

Potentiometric Titration of the Amino Derivatives of Benzimidazole

The potentiometric titration of these compounds was conducted with a vacuum tube potentiometer of the system GIPKh with glass electrodes [12]. The values of the basic constants found are given in the theoretical part of the present communication.

Figs. 1 and 2 give the curves obtained upon the potentiometric titration of the isomeric amino-2-methylbenzimidazoles.

SUMMARY

Derivatives of 4-aminobenzimidazole were prepared by the condensation of consecutive triaminobenzene with organic acids, whose chemical properties were compared with those of the 5-aminobenzimidazoles. These products were studied by the method of potentiometric titration. The results obtained were compared with those of experiments on nitration and azo coupling of these substances.

It was shown that derivatives of 4-amino- and 5-aminobenzimidazole differ sharply from each other in chemical properties. Whereas the amino group in position 4 does not interact with the imidazole ring and strongly activates the benzene ring, that in position 5 greatly affects the imidazole ring and practically does not activate the benzene ring of these compounds.

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SYNTHESIS OF γ-SUBSTITUTED PYRIDINES

M. V. Rubtsov, E. S. Nikitskaya, and A. D. Yanina

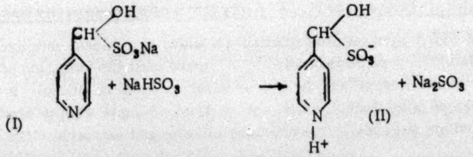
γ-Substituted pyridines are considered poorly accessible compounds because of difficulties connected with the isolation of pure γ-picoline which is contained in the β-picoline fraction along with β-picoline and α,α-lutidine. However, these difficulties can be removed by using specific properties of the components of the β-picoline fractions. After the removal of α,α-lutidine, readily accomplished with the aid of zinc chloride, it is fully possible, using the differences in reactivity of the methyl groups found in the β- and γ-positions, to choose such conditions with which a differential reaction will proceed. In particular, the possibility of oxidizing γ-picoline to γ-formylpyridine in the presence of β-picoline was of interest.

Up to now, there was no convenient method for the preparation of γ-formylpyridine [1] reported in the literature. Nevertheless, this compound is of considerable interest for the synthesis of a whole series of pyridine derivatives.

The experiments conducted showed that the differential oxidation of γ-picoline in the presence of β-picoline was possible.

The properties of γ-formylpyridine were investigated, and the condensation reaction with malonic acid and ester was studied.

Upon treating a toluene solution of γ-formylpyridine with a 50% sodium bisulfite solution, a white finely crystalline powder precipitated which was a mixture of sodium γ-pyridylhydroxymethanesulfonate and sodium bisulfite. Upon the crystallization of the mixture obtained from water, white needle-like crystals not containing sodium and which were the internal salt of γ-pyridylhydroxymethanesulfonic acid, were formed. The formation of the internal salt occurs according to the scheme:



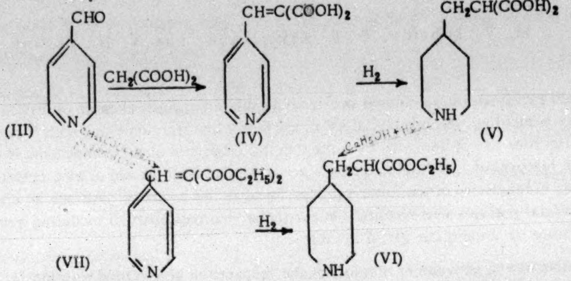
which was confirmed by the reaction of a specially prepared pure sodium γ-pyridylhydroxymethanesulfonate with an equimolecular amount of sodium bisulfite. An analogous transformation occurred by the action of acetic acid. The formation of an internal salt is also known for α-formylpyridine [2].

For the separation of the free aldehyde (III) the sodium γ-pyridylhydroxymethanesulfonate was heated for a short time with 35% potassium carbonate solution, extracted with ether or chloroform, and dried with potassium carbonate. If the solvent was distilled off, then a small amount of a sharp-smelling liquid with b.p. 185-187° remained, which rapidly crystallized in the air. The crystals were a compound of γ-formylpyridine with 1 mol. of water.

A considerable part of the aldehyde distilled together with the solvents, which could be detected by the addition of an alcoholic solution of hydrogen chloride to the distillate; the hydrochloride of γ-formylpyridine precipitated in the form of a white, flocculant residue.

The hydrochloride crystallized with 0.5 mol. of water which could not be removed at 100° in vacuum. The anhydrous hydrochloride could only be obtained by vacuum distillation.

γ-Formylpyridine hydrochloride readily condensed with malonic acid and ester. The condensation with malonic acid proceeded in a glacial acetic acid medium at 85-90° with the formation of 4-(β,β-dicarboxylvinyl) pyridine (IV). The condensation with malonic ester proceeded in a pyridine medium in the presence of a small excess of piperidine (2-3 % over the equimolecular amount) with the formation of 4-(β,β-dicarbethoxyvinyl)pyridine (VII). The reaction occurred in the cold upon prolonged standing. Heating did not accelerate the process or increase the yield.



4-(β,β-Dicarboxyvinyl)pyridine (IV) was partly decarboxylated by heating with an alcoholic hydrogen chloride solution, which was shown by the precipitation of ethyl β-(pyridyl-4)-acrylate from the reaction mixture. For this reason, 4-(β,β-dicarbethoxyyinyl)pyridine (VII) could not be obtained by esterification. (VII) also could not be obtained by means of the acid chloride, since thionyl chloride reacted with 4-(β,β-dicarboxyvinyl)pyridine only at 70-75°, at which a partial decarboxylation occurred.

Much more stable is 4-(β,β-dicarboxyethyl)piperidine (V) which was readily obtained by the hydrogenation of (IV) hydrochloride in 4% hydrochloric acid in the presence of a platinum catalyst (according to Adams).

4-(β,β-dicarbethxoxyethyl)piperidine (VI) was formed in good yield by the esterification of (V). Hydrogenation of (VII) over a platinum catalyst in absolute alcohol also led to the formation of (VI). The latter compound was converted into 2-quinuclidinecarboxylic acid by means of the corresponding bromo derivative [3].

EXPERIMENTAL

Isolation of the Internal Salt of γ-Pyridylhydroxymethanesulfonic acid (II).

10 ml of a 50% sodium bisulfite solution was added to a toluene solution of 2.42 g of γ-formylpyridine, obtained by the oxidation of γ-picoline, cooled to 0°, stirred until the formation of mushy mass on the bottom of the beaker, the liquid poured from it, and the residue added to 50 ml of alcohol. It was thoroughly mixed and filtered. The residue was washed with alcohol, ether, and air dried. 7.3 g of a white crystalline powder was obtained which was a mixture of sodium γ-pyridylhydroxymethanesulfonate and sodium bisulfite.

Upon recrystallization from water, white, shiny, needlelike crystals of the internal salt of γ-pyridylhydroxymethanesulfonic acid were obtained. The substance is readily soluble in hot water, moderately in the cold; it is insoluble in the common organic solvents and does not melt.

3.470 mg substance: 4.831 mg CO_2; 1.247 mg H_2O. 6.371 mg substance: 3.37 ml 0.01 N H_2SO_4. 0.1615 g substance: 0.1910 g $BaSO_4$. Found %: C 37.99; H 4.02; N 7.41; S 16.85. $C_6H_7O_4NS$. Calculated %: C 38.09; H 3.70; N 7.40; S 16.93.

Conversion of the Internal Salt of γ-Pyridylhydroxymethanesulfonic Acid into the Sodium Salt and the Reverse.

2.25 ml of a 1N solution of sodium hydroxide was added to 0.56 g of the internal salt of γ-pyridylhydroxymethanesulfonic acid, 50 ml of absolute alcohol was added to the solution formed, and shaken. The precipitated residue was filtered, washed with ether, and dried in vacuum. Weight of the residue, 0.59 g. Yield, 95 % of the theoretical.

0.1049 g substance: 0.1199 g $BaSO_4$. 0.1044 g substance: 0.0325 g Na_2SO_4. Found %: S 15.69; Na 10.91. $C_6H_6O_4NSNa$. Calculated %: S 15.16; Na 10.90.

0.17 g of dry sodium bisulfite, freshly precipitated from a 50% alcoholic solution with alcohol, was added to 0.33 g of sodium γ-pyridylhydroxymethanesulfonate obtained from the internal salt. The mixture was recrystallized from water. The precipitate was washed with alcohol and ether, and dried in vacuum at 120°. 0.25 g of the substance was obtained. Yield, 85 % of the theoretical.

3.563 mg substance: 4.940 mg CO_2; 1.316 mg H_2O. 6.834 mg substance: 3.47 ml 0.01 N H_2SO_4. Found %: C 37.83; H 4.13; N 7.10. $C_6H_7O_4NS$. Calculated %: C 38.09; H 3.70; N 7.40.

γ-Formylpyridine Thiosemicarbazone

If the toluene filtrate, containing 3.1 g of γ-formylpyridine was stirred for one hour with a solution of 2.63 g of thiosemicarbazide in 13 ml of water at 70-75°, a greenish crystyalline precipitate with m.p. 213-214° formed. The residue was poorly soluble in alcohol, insoluble in water, acetone, and ether. Yield 5 g or 96 % of the theoretical. After recrystallization from alcohol, the substance melted at 215-217° with decomposition [4].

6.135 mg substance: 7.971 mg $BaSO_4$. Found %: S 17.84. $C_7H_8N_4S$. Calculated %: S 17.78.

Upon treating the thiosemicarbazone with 10% hydrochloric acid, a bright yellow precipitate which was the thiosemicarbazone hydrochloride, melted at 238.5-239.5° after recrystallization from 50% alcohol. If dissolved in cold water at a ratio of 1:90, it was precipitated from the solution with an excess of hydrochloric acid.

0.2262 g substance: 0.2402 g $BaSO_4$. Found %: S 14.58. $C_7H_8N_4S \cdot HCl$. Calculated %: S 14.78.

Isolation of Free γ-Formylpyridine (III)

7.6 g of the impure sodium salt of γ-pyridyl hydroxymethanesulfonic acid was heated on the water bath for 5 minutes with 15 ml of water and 30 ml of a 50% potassium carbonate solution. The precipitate went into solution, and the sharp characteristic odor appeared.

The hot solution was rapidly extracted with chloroform (in ether, the aldehyde is less soluble). The chloroform extract was dried with potassium carbonate and evaporated in vacuum. 1.56 g of a colorless, mobile liquid remained which distilled at 185-187° and was γ-formylpyridine. The compound obtained was characterized by its volatility, and a considerable amount is transferred into the distillate upon evaporation of the solution.

γ-Formylpyridine rapidly absorbed moisture from the air and was converted into a crystalline compound melting at 58-60°. The crystallohydrate dissolves readily in water and alcohol, less in ether.

3.990 mg substance: 8.481 mg CO_2; 2.267 mg H_2O. 4.752 mg substance: 10.103 mg CO_2; 2.371 mg H_2O. 4.308 mg substance: 4.34 ml 0.01 N H_2SO_4. 5.912 mg substance: 4.80 ml 0.01 N H_2SO_4. Found %: C 57.96, 57.98; H 5.82, 5.58; N 11.44, 11.38. $C_6H_5ON \cdot H_2O$. Calculated %: C 57.60; H 5.60; N 11.20.

2.09 g of γ-formylpyridine hydrochloride was formed from the chloroform distillate by means of an alcoholic solution of hydrogen chloride. The total yield, based on the sodium salt of γ-pyridylhydroxymethanesulfonic acid, was 78% of the theoretical. γ-Formylpyridine hydrochloride was a white powder, readily soluble in water and alcohol, poorly in chloroform, and insoluble in ether. It contained 0.5 mol. of water. M.p. 132-134°.

5.800 mg substance: 0.469 ml N_2 (25°, 730.5 mm). 5.143 mg substance: 0.422 ml N_2 (25°, 730.5 mm). 4.597 mg substance: 4.381 mg AgCl. 5.989 mg substance: 5.702 mg AgCl. Found %: N 8.90, 9.03; Cl 23.59, 23.55. $C_6H_5ON \cdot HCl \cdot 0.5\ H_2O$. Calculated %: N 9.18; Cl 23.28.

γ-Formylpyridine hydrochloride was distilled in vacuum upon heating and lost its water of crystallization. The anhydrous hydrochloride melted at 159.5-161.5°. However, it rapidly absorbed water and was again converted into the compound with m.p. 132-134°.

8.00 mg substance: 0.684 ml N_2 (21°, 728.5 mm). Found %: N 9.52. $C_6H_5ON \cdot HCl$. Calculated %: N 9.75.

4-(β,β-Dicarboxyvinyl)pyridine (IV).

3.1 g of γ-formylpyridine hydrochloride, 2.26 g of malonic acid, and 7.5 ml of glacial acetic acid were heated with stirring on the water bath to 85-90°. Everything went into solution at 40-50°, while at 80-85°, a precipitate began to form. It was stirred at 85-90° for 45 minutes, filtered, washed with glacial acetic acid and then with ether, and air dried. 3.8 g of 4-(β,β-dicarboxyvinyl) pyridine hydrochloride with m.p. 219-220° was obtained. Yield 81% of the theoretical. The substance was soluble in water, and insoluble in alcohol, ether, and acetic acid.

3.448 mg substance: 5.993 mg CO_2; 1.133 mg H_2O. 3.619 mg substance: 2.278 mg AgCl. 6.289 mg substance; 3.906 mg AgCl. Found %: C 47.40; H 3.67; Cl 15.57, 15.37. $C_9H_7O_4N \cdot HCl$. Calculated %: C 47.05; H 3.48; Cl 15.47.

In order to separate the free 4-(β,β-dicarboxyvinyl)pyridine, the hydrochloride was mixed with an equivalent amount of sodium acetate in aqueous solution. The precipitate which came out was filtered, washed with water, alcohol, and ether, and air dried.

4-(β,β-Dicarboxyvinyl)pyridine was not soluble in water or in the usual organic solvents. M.p. 263-265° (with decomposition). It crystallized with 1.5 mol. of water.

7.533 mg substance: 3.50 ml 0.01 N H_2SO_4. 5.640 mg substance: 2.61 ml 0.01 N H_2SO_4. Found %: N 6.54, 6.48. $C_9H_7O_4N \cdot 1.5H_2O$. Calculated %: N 6.36.

Upon drying in vacuum at 100°, 4-(β,β-dicarboxyvinyl)pyridine loses its crystallization water.

4.936 mg substance: 2.58 ml 0.01 N H_2SO_4. 3.126 mg substance: 1.62 ml 0.01 N H_2SO_4. Found %: N 7.32, 7.25. $C_9H_7O_4N$. Calculated %: N 7.25.

4-(β,β-Dicarboxyethyl)piperidine (V).

A solution of 4-(β,β-dicarboxyvinyl)pyridine hydrochloride in 50 ml of hydrochloric acid was hydrogenated at room temperature in the presence of 0.3 g of platinum oxide at 40-60 mm of water pressure. The absorption was completed in 5-6 hours. The catalyzate was filtered, washed with a small amount of distilled water, filtered, evaporated in vacuum at 30° until a slurry was obtained, the residue filtered, washed with absolute alcohol and ether, and dried in a vacuum desiccator. Coarse, shiny, colorless crystals with m.p. 237-239° were obtained in a 3.27 g quantity. Yield 91 % of the theoretical. The substance was readily soluble in water, difficultly in alcohol, and insoluble in ether.

3.072 mg substance: 5.128 mg CO_2; 1.871 mg H_2O. 5.032 mg substance: 5.030 mg AgCl. Found %: C 45.52; H 6.81; Cl 14.90. $C_9H_{15}O_4N \cdot HCl$. Calculated %: C 45.47; H 6.74; Cl 14.94.

In order to separate the free 4-(β,β-dicarboxyethyl)piperidine, the hydrochloride was mixed with an equivalent amount of sodium acetate and a small amount of water. The residue obtained was washed with water, alcohol, and ether, and dried in a vacuum desiccator. 4-(β,β Dicarboxyethyl)piperidine was obtained in the form of white fine crystals with m.p. 255.5-256° (with decomposition). The substance was readily soluble in water.

5.247 mg substance: 2.50 ml 0.01 N H_2SO_4. Found %: N 6.67. $C_9H_{15}O_4N$. Calculated %: N 6.96.

4-(β,β-Dicarbethoxyethyl)piperidine (VI).

8 g of 4-(β,β-dicarboxyethyl)piperidine hydrochloride was heated with 80 ml of a 4% alcoholic solution of hydrogen chloride for 2 hours with boiling, and the alcohol was then removed in vacuum. The residue was heated with a fresh portion of 4% alcoholic hydrogen chloride solution for 2 hours more, the alcohol removed in vacuum, the residue treated with an excess of a 50% potassium carbonate solution, and extracted with ether. The ether extract was dried with potassium carbonate, filtered, and treated with an alcoholic solution of hydrogen chloride to a weakly acid solution on Congo. The precipitated shiny residue was filtered, washed with ether, and dried in a vacuum desiccator. 7.8 g of 4-(β,β-dicarbethoxyethyl)piperidine hydrochloride with m.p. 128-129° [3] was obtained. Yield 79.5% of the theoretical. The substance was readily soluble in water, alcohol, chloroform, and insoluble in ether.

3.805 mg substance: 7.448 mg CO_2; 2.665 mg H_2O. 3.841 mg substance: 7.516 mg CO_2; 2.654 mg H_2O. 7.147 mg substance: 2.52 ml 0.01 N H_2SO_4. Found %: C 53.38, 53.37; H 7.84, 7.73; N 4.94. $C_{13}H_{23}O_4N \cdot HCl$. Calculated %: C 53.15; H 7.80; N 4.77.

4-(β,β-Dicarbethoxyvinyl)pyridine (VII)

3.3 g of γ-formylpyridine ester, 3.53 g of malonic ester 8.6 ml of pyridine, and 3.3 ml of piperidine, were left to stand in a closed flask for 4 days at room temperature (about 15°). The precipitated residue of piperidine hydrochloride was filtered, the filtrate was evaporated in vacuum at 50°, the residue was diluted with 60 ml of dry ether, the precipitated piperidine hydrochloride was filtered once, the ether filtrate was washed with 15% sodium carbonate solution, and dried with potassium carbonate. The ether was removed, and the residue was vacuum distilled, collecting the fraction with b.p. 176-178° at 7 mm. Yield 3.3 g, or 62% of the theoretical.

In order to prepare the hydrochloride, the compound obtained was dissolved in absolute ether, and a solution of hydrogen chloride in alcohol added, to a weakly acidic reaction on Congo. 3.6 g of a substance with m.p. 180-182° [3] was obtained after many recrystallizations from alcohol. The yield of the hydrochloride based on the ether was 97% of the theoretical.

7.221 mg substance: 2.49 ml 0.01 N H_2SO_4. 7.140 mg substance: 2.15 ml 0.01 N H_2SO_4. 3.948 mg substance: 2.101 mg AgCl. Found %: N 4.82, 4.90; Cl 12.53. $C_{13}H_{15}O_4N \cdot HCl$. Calculated %: N 4.90; Cl 12.42.

4-(β,β Dicarbethoxyethyl)piperdine [3] was obtained by the hydrogenation of 4-(β,β-dicarbethoxyvinyl) pyridine hydrochloride in absolute alcohol over platinum oxide.

SUMMARY

A series of γ-formylpyridine derivatives was prepared and their condensation with malonic acid and ester was studied.

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SYNTHESES BASED UPON ANABASINE

V. STUDY OF THE TRANSFORMATION PRODUCTS OF N-(β-HYDROXYETHYL)ANABASINE

A. S. Sadykov, O. S. Otroshchenko, and M. K. Yusupov

The synthesis of anabasine amino alcohols and the transformations of N-(β-hydroxyethyl)anabasine were reported in the previous communications [1, 2]. The experimental data of the chemical characteristics of N-(β-hydroxyethyl)anabasine, and the products of its transformation are given in the present communication.

Reagents: anabasine, 16 g, ethylene oxide, 4.35 g. Reaction conditions: temperature, 18-20°, volume of solvent, 50 ml.

Solvent	Experiment time (in hrs.)	Yield of N-(β-hydroxyethyl)anabasine (in %)	Amount of anabasine recovered (in %)
Methyl alcohol	24	36	57
Methyl alcohol	48	39.8	50
Methyl alcohol	96	43	29
Absolute ethyl alcohol	24	40	55
" " "	36	47	47
" " "	48	59	28
" " "	96	70	13

The anabasine (I) used for the investigation was obtained and purified as reported previously [3]. The reaction of anabasine with ethylene oxide was accomplished at room temperature in methyl and ethyl alcohol solutions at various reaction times, with the reagents used in equimolecular amounts. The results obtained are given in the Table.

As is apparent from the data given, better yields of N-(β-hydroxyethyl)anabasine (II) were obtained in absolute alcohol with a reaction time of 96 hours.

N-(β-Hydroxyethyl)anabasine was characterized by the preparation of salts: the hydroiodide with m.p. 204-205°, the hydrochloride with m.p 193-194°, the picrate with m.p. 180-181°, the phenylurethane with m.p. 143-144°, and the acetyl derivative [4].

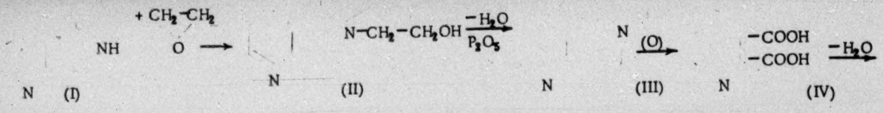
During a study of the dehydration reaction of N-(β-hydroxyethyl)anabasine with phosphoric anhydride, a crystalline product with m.p. 53-54° was isolated containing condensed lupinine and pyridine rings. The new compound was called 4,5-(α, β-pyridylene)norlupinane (III). It was readily soluble in organic solvents (ether, chloroform, benzene), and more poorly, in water. It gives a crystalline picrate with m.p. 201-202°.

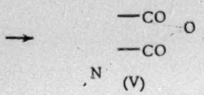
A series of experiments showed that the optimum temperature conditions for the dehydration of N-(β-hydroxyethyl)anabasine with phosphoric anhydride lie within the limits 120-130° (Yield 16.5%). Below 120°, the reaction did not occur. Above 140°, the reaction proceeds with strong tarring, which is, evidently, due to the polymerization of vinylanabasine formed during the reactionprocess.

The structure of 4,5-(α, β-pyridylene)norlupinane (III) was proved by its oxidation with potassium permanganate; a dibasic acid was isolated with m.p. 229-230°. A study of the properties of this acid (IV) [5] and its anhydride (V) [6], made it possible to conclude quinolinic acid was formed by this reaction. A direct comparison of the acid with the quinolinic acid obtained by the oxidation of quinoline showed their identity.

The formation of quinolinic acid during the oxidation of 4,5-(α, β-pyridylene)norlupinane showed that during the dehydration of N-(β-hydroxyethyl)anabasine with phosphoric anhydride the ring closure occurs by means of the hydroxyl of the side chain and the hydrogen of α-carbon atom of the pyridine ring.

The preparation of N-(β-hydroxyethyl)anabasine and its chemical transformations can be represented by the following scheme:





EXPERIMENTAL

Reaction of Anabasine (I) with Ethylene Oxide

49 g (1.11 moles) of ethylene oxide was passed with cooling and shaking into a solution of 180 g (1.11 moles) of anabasine in 360 ml of absolute alcohol. The reaction mass was left to stand at room temperature. After 96 hours, the alcohol was distilled from it, and the residue (a dark oil) was vacuum distilled. Two fractions were obtained: 1) b.p. 110-127° (2 mm), 43.7 g (24.3 %), anabasine; 2) b.p. 142-144° (2 mm), 146.6 (64.0%), N-(β-hydroxyethyl)anabasine. The second fraction was redistilled at 174-176° (5 mm) in the form of a thick oil.

Phenylurethane. 0.55 g of phenyl isocyanate was added to a solution of 1 g N-(β-hydroxyethyl)anabasine (II) in 12 ml of dry petroleum ether with shaking. The mixture was heated for several minutes on the water bath. A crystalline substance precipitated on standing, which was filtered and washed with a small amount of absolute ether. After recrystallization from alcohol, the phenylurethane had an m.p. 143-144°.

2.550 mg substance: 0.322 ml N_2 (25°, 721 mm). 2.954 mg substance: 0.372 ml N_2 (28°, 720.5 mm). Found %: N 12.97, 13.14. $C_{19}H_{23}O_2N_3$. Calculated %: N 12.91.

The picrate precipitated upon mixing alcoholic solutions of N-(β-hydroxyethyl)anabasine and picric acid. After recrystallization from alcohol, the m.p. was 180-181°.

The hydrochloride was obtained in the form of a thick oil upon mixing acetone solutions of N-(β-hydroxyethyl)anabasine and hydrogen chloride. The oil was converted into crystals upon standing. After recrystallization from a mixture of alcohol and acetone, it had an m.p. 193-194°.

The hydroiodide was obtained by adding a solution of hydriodic acid to a solution of N-(β-hydroxyethyl)anabasine in methyl alcohol.

Acetyl Derivative of N-(β-Hydroxyethyl)anabasine.

14 g (0.07 mole) of N-(β-hydroxyethyl)anabasine and 8.0 g (0.13 mole of acetic anhydride dissolved in 120 ml of pyridine were heated on the boiling water bath using a reflux condenser equipped with a calcium chloride tube for 4 hours. The pyridine and excess anhydride were removed and the residue was vacuum distilled. A fraction with b.p. 179-183° (2 mm) was obtained; yield 14.1 g (83.7%). The substance was an oil readily soluble in organic solvents (ether, benzene, acetone, alcohol), and poorly soluble in water.

Dehydration of N-(β-Hydroxyethyl)anabasine

A mixture of 10 g of N-(β-hydroxyethyl)anabasine and 9 g of phosphoric anhydride was heated on a oil bath for 2 hours at 120-130° in a flask with a reflux condenser (equipped with a calcium chloride tube.) The reaction product was dissolved in a small volume of hot water and was treated with a 40% sodium hydroxide solution. The alkaline solution was saturated with potassium carbonate and extracted with chloroform. The tarry mass obtained after the removal of the chloroform was dissolved in acetone. A white crystalline precipitate with m.p. 53-54° formed in the acetone solution on standing. The yield of 4,5-(α,β-pyridylene)norlupinane (III) was 1.05 g, 16.4% of the theoretical.

Oxidation of 4,5-(α,β-pyridylene)norlupinane. 0.35 g of 4,5-(α,β-pyridylene)norlupinane in 20 ml of water was mixed with a solution of 2.5 g of potassium permanganate in 70 ml of water. The solution was heated for several hours on the boiling water bath. The excess of the oxidizing agent was then decolorized by the addition of alcohol. The filtrate after the removal of the manganese dioxide, was evaporated on the water bath to a small volume and neutralized with 15% hydrochloric acid. The acid was precipitated from the neutralized solution as the copper salt by the addition of copper acetate. The copper salt obtained was decomposed with hydrogen sulfide. The filtrate after the removal of the copper sulfide precipitate, was evaporated to a small volume until the formation of crystals started. The precipitated crystals were filtered and recrystallized from hot water with the addition of active carbon. The quinolinic acid obtained was crystalline substance with m.p. 228-229°. Yield, 0.21 g (67.7%).

1.932 mg substance: 0.168 ml N_2 (25°, 723 mm). 2.426 mg substance: 0.202 ml N_2 (28°, 723 mm). Found %: N 9.09, 8.60. $C_7H_5O_4N$. Calculated %: N 8.38.

11.015 mg acid: 1.33 ml 0.1 N NaOH. 8.368 mg acid: 1.03 ml 0.1 N NaOH. Found: Equivalent 84.7, 83.1. $C_7H_5O_4N$. Calculated: Equivalent 83.5.

Acid anhydride. 62 mg of the finely ground quinolinic acid obtained by the oxidation of N-(β-hydroxyethyl) anabasine in 200 mg of acetic anhydride was heated on an oil bath at 120-125° until complete solution of the acid. Then after a short heating at 150°, the reaction product was cooled and dissolved in carbon tetrachloride. On standing, slow precipitation of a crystalline product started in the solution. On the following day, the crystals were filtered and washed with carbon tetrachloride. Crystals in the form of shiny prisms with m.p. 133-134° were obtained after drying. Upon heating the anhydride with resorcin on the water bath, a yellow fluorescent color was obtained. This is a characteristic reaction for quinolinic anhydride (V).

SUMMARY

1. The reaction of equimolar amounts of anabasine and ethylene oxide in methyl and absolute ethyl alcholic media was studied. The best yields (69%) of N-(β-hydroxyethyl)anabasine were obtained by conducting the reaction in absolute alcohol at room temperature for 96 hours.

2. The hydroiodide with m.p. 204-205°, the hydrochloride with m.p. 193-194°, the picrate with m.p. 180-181°, and the phenylurethane with m.p. 143-144° were prepared to characterize the N-(β-hydroxyethyl)anabasine.

3. The dehydration reaction of N-(β-hydroxyethyl)anabasine by phosphoric anhydride was studied. A new compound called 4,5-(α,β-pyridylene)norlupinane (III) was obtained. The structure of this compound was proved by oxidation to quinolinic acid and the preparation of the anhydride of the latter. It was shown that the dehydration of N-(β-hydroxyethyl)anabasine occurs by means of the hydroxyl group of the alcohol and the hydrogen of the α-position of the pyridine ring.

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* See Consultants Bureau Translation p. 2135.

SYNTHESIS OF N,O-PEPTIDES OF SERINE

M. M. Botvinik, S. M. Avaeva, and E. A. Mistryukov

In relation to the study of the role of the hydroxyl in proteins, it was found necessary to synthesize peptides of serine, not only with the amino, but also with the hydroxyl group.

More than once it has been suggested in the literature that ester linkages existed in proteins, or more accurately, in systems of proteins [1]. But this suggestion has only been a hypothesis up to now, unproved experimentally. For the experimental solution of this problem, it was necessary to initially study the properties of ester linkages formed by aminoacids and the hydroxyl groups of β-hydroxyamino acids.

For this purpose, methods of synthesis were developed during the present investigation and a series of N,O-peptides of serine was obtained.

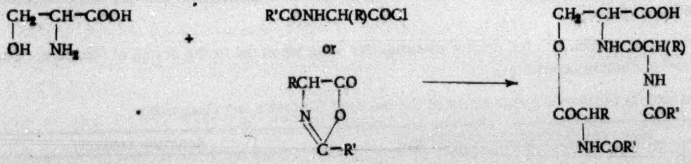
The N,O-peptides are considered to be those formed by the amino and hydroxyl groups of β-hydroxyamino acids.

The number of synthesized peptides of β-hydroxyamino acids is very small [8]. The first peptide of threonine was first synthesized in 1950 [2], while the N,O-peptides are scarcely studied. In the majority of cases, they have only been obtained as side products during the synthesis of peptides of hydroxyamino acids.

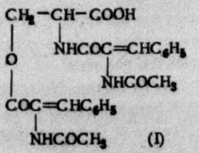
Thus in 1927, N,O-di(acetyldehydrophenylalanyl)serine was obtained during the condensation of serine with 2-methyl-4-benzal-5-oxazolone in addition to the N-peptide, which was not studied further by the authors [3].

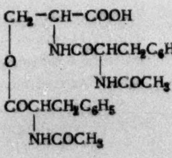
N,O-dityrosylserine was obtained in 1932 [4], and in 1949, at the conclusion of the present investigation, a communication appeared on the synthesis of the ethyl ester of O-(N-benzoylphenylalanyl)-N-benzoylserine [5]. These concluded the investigations on N,O-peptides of β-aminohydroxy acids.

The reaction between acylated amino acid halides and oxazolones of serine and its derivatives was used for the synthesis of N,O-peptides of serine:



Initially, the above reaction was applied to the condensation of 2-methyl-4-benzal-5-oxazolone with serine. The yield of N,O-diacetyldehydrophenylalanylserine (I) was increased by varying several of the reaction conditions. The latter compound was hydrolyzed by hydrogen over palladium. N,O-diacetylphenylalanylserine (II) was first obtained by the authors as a result:

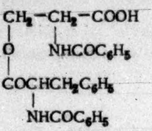

(I)

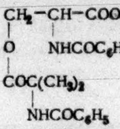

(II)

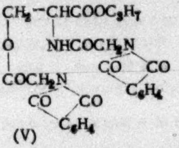
However, this method was limited by the poorly accessible unsaturated oxazolones with aliphatic radicals in the 4-position and the many stages in the synthesis. For this reason, investigations were conducted on the synthesis of N,O-peptides of serine with acylated amino acid halides and saturated oxazlones.

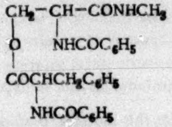
The first experiments conducted in this direction, led to negative results [6]: hippurylchloride did not react with benzoylserine or benzoyltheonine in ether and benzene media.

After varying the experimental conditions, in particular, the conducting of the experiments in homogenous medium, the following N,O-peptides and N-acyl-O-peptides of serine were synthesized: O-(benzoylphenylalanyl)-N-benzoylserine (III), by the action of N-benzoylphenylalanyl chloride on benzoylserine, yield 40 %; the ethyl ester of O-(benzoylaminoisobutyryl)-N-benzoylserine (IV), by the action of N benzoylaminoisobutyryl hydrochloride on the ethyl ester of N-benzoylserine, yield 18%; the isopropyl ester of N,O-diphthalylglycylserine (V), by the action of N-phthalylglycyl chloride on the isopropyl ester of serine, yield, 69%; and the methylamide of O-(benzoylphenylalanyl)-N-benzoylserine (VI), by the action of N-benzoylphenylalanyl chloride on the methyl amide of N-benzoylserine, yield 77%.


(III)

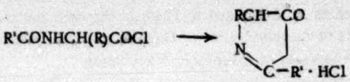

(IV)


(V)


(VI)

In addition to the acylated amino acid chlorides, the corresponding oxazolones were also used. But these oxazolones react much less readily with serine and its derivatives, and N,O-peptides could not be obtained in these cases. Thus, for example, benzoylserine reacted with benzoylphenylalanyl chloride to form O-(benzoylphenylalanyl)-N-benzoylserine. The reaction did not occur with 2-phenyl-4-benzyl-5-oxazolone. The Table gives the experiments conducted. They prove the above-mentioned facts that oxazolones react less readily than acylated amino acid chlorides. The latter also react non-uniformly.

Now it can be considered proved that acyl amino acid chlorides spontaneously are transformed into oxazolone hydrochlorides, which are also capable of reacting with amine and hydroxyl groups:



Evidently, acylated amino acid chlorides are much more reactive than oxazolone hydrochlorides. This is particularly shown by the fact that phthalylglycyl chloride, which cannot be transformed into the salt of oxazolone, reacted exceptionally readily with serine.

The N,O-peptides obtained in the present investigation were subjected to the action of ferments. The results are reported in another communication [7].

Reaction of Serine and its Derivatives with Acylated Amino Acid Chlorides and Oxazolones.

Names of the reaction components		Reaction products
1	2	3
Serine	2-Methyl-4-benzal-5-oxazolone	N,O-di-(acetyldehydrophenylalanyl) serine
Isopropyl ester of serine (hydrochloride)	Phthalylglycyl acid chloride	Isopropyl ester of N,O-di-(phthalylglycyl)serine
Benzoylserine	2-Phenyl-4-benzyl-5-oxazolone	Reaction did not occur
Benzoylserine	Benzoylphenylalanyl acid chloride	O-(benzoylphenylalanyl)-N-benzoylserine
Ethyl ester of benzoylserine	2-Phenyl-4,4-dimethyl-5-oxazolone	Reaction did not occur
Ethyl ester of benzoylserine	Benzoylaminoisobutyryl acid chloride	Ethyl ester of O-(benzoylaminoisobutyryl)-N-benzoylserine
Methylamide of benzoylserine	Benzoylphenylalanyl acid chloride	Methylamide of O-(benzoylphenylalanyl)-N-benzoylserine

EXPERIMENTAL

Synthesis of N,O-di-(acetylphenylalanyl)serine (II)

a) Preparation of N,O-di-(acetyldehydrophenylalanyl)serine (I) 9.35 g of 2-methyl-4-benzal-5-oxazolone dissolved in 65 ml of acetone was added to a solution of 5.25 g of serine in 42 ml of 1.2 N alkali. The mixture was shaken for 3 hours, the undissolved oxazolone was filtered off, and the filtrate was evaporated in vacuum. The oil which precipitated at the start of the evaporation was separated (substance A). The filtrate was evaporated to dryness in vacuum (substance B).

Substance A crystallized upon standing. The crystals obtained were treated with boiling benzene, and then recrystallized from aqueous alcohol. N,O-Di-(acetaldehydrophenylalanyl)serine with m.p. 196° was obtained. According to literature data, m.p. 202° [3].

Substance B (6.6 g) was dissolved in absolute alcohol for separation from sodium chloride. The filtrate was evaporated to half of its volume and filtered once more. After evaporation to dryness, a substance remained which was in the form of light yellow shiny platelets. It was dissolved in a mixture of alcohol and ethyl acetate and precipitated with petroleum ether. N-(Acetyldehydrophenylalanyl)serine with m.p. 173° was obtained. According to literature data, m.p. 178° [3].

Found: equiv. 328, 324. Calculated: equiv. 292.

b) Hydrogenation of N,O-di(α-acetyldehydrophenylalanyl)serine. 2.8 g of N,O-di-(α-acetyldehydrophenylalanyl)serine was dissolved in absolute methyl alcohol and hydrogenated with hydrogen over palladium black for 18 hours. 275 ml of hydrogen were absorbed (theoretical amount 262 ml). The solution was evaporated in a vacuum after the removal of the catalyst. The oil which precipitated crystallized upon strong cooling and prolonged standing. N,O-Di-(α-acetylphenylalanyl) serine melted at 82-85°. Yield 2.25 g, 79.8 % of the theoretical.

The compound has not been reported in the literature.

Found %: C 60.70, 60.53; H 6.48, 6.43; N 8.67, 8.56. $C_{25}H_{29}O_7N_3 \cdot \frac{1}{2}H_2O$. Calculated %: C 60.97; H 6.09; N 8.53.

After drying in vacuum at 80° (5 mm) over phosphoric anhydride, m.p. 103- 105°.

Found %: C 61.67, 61.58; H 6.17, 6.18; N 8.72, 8.72. $C_{25}H_{29}O_7N_3$. Calculated %: C 62.11; H 6.09; N 8.69.

c) Preparation of N-(acetylphenylalanyl)serine. 2 g of N-(acetyldehydrophenylalanyl)serine in methyl alcohol solution was hydrogenated for 5 hours with hydrogen over palladium black. 210 ml of hydrogen was absorbed (theoretical amount 196 ml). After the removal of the catalyst and washing with alcohol, the filtrate was concentrated in vacuum. The substance solidified in the form of shiny scales.

M.p. 76-78°. Yield of N-(acetylphenylalanyl)serine was 1.9 g, 95% of the theoretical.

The substance was dried in vacuum at 56° over phosphoric anhydride.

Found %: C 54.72, 54.59; H 6.28, 6.24; N 8.85, 8.88. $C_{14}H_{18}O_5N_2 \cdot \frac{1}{2}H_2O$. Calculated %: C 55.47; H 6.27; N 9.20.

Reaction of the Ethyl Ester of N-Benzoylserine with 2-Phenyl-4,4-dimethyl-5-oxazolone

A solution of 0.24 g of the ethyl ester of N-benzoylserine (m.p. 85°) and 0.27 g of 2-phenyl-4,4-dimethyl-5-oxazolone in absolute toluene were heated for 3 hours at 65-70° and for 3 hours at the boiling point of toluene. The toluene was removed in vacuum and aniline was added to the residue to remove the unreacted oxazolone. After a 5 minute heating, at 50-60°, the reaction mass solidified. The residue, recrystallized from benzene, was benzoylaminoisobutyric acid anilide (0.3 g). M.p. 227°.

The aniline was removed from the mother liquor with hydrochloric acid, and benzoylserine ethyl ester was isolated. Therefore, the reaction between the ethyl ester of N-benzoylserine and 2-phenyl-4,4-dimethyl-5-oxazolone did not occur.

Synthesis of the Ethyl Ester of O-(Benzoylaminoisobutyryl)-N-Benzoylserine (IV)

2g of N-benzoylserine ester and 2.25 g of benzoylaminoisobutyryl acid chloride in chloroform solution were heated for 8 hours on the water bath at 60-65°. The undissolved residue was filtered off, and the filtrate evaporated in vacuum. The residual oil was dissolved in alcohol, and water was added dropwise to the solution until a cloudiness appeared. The ethyl ester of O-(benzoylaminoisobutyryl)-N-benzoylserine was isolated in the form of long white needles. Yield 0.5 g. M.p. 128°.

The compound has not been reported in the literature.

Found %: C 65.40, 65.49; H 6.14, 6.14; N 6.75, 6.83. $C_{23}H_{26}O_6N_2$. Calculated %: C 65.40; H 6.16; N 6.63.

Hydrolysis of the Ethyl Ester of O-(Benzoylaminoisobutyryl)-N-benzoylserine (IV). The amounts of the substances given below were treated with 8 ml of 1/40 N alkali and boiled on the water bath for 3 hours. 8 ml of 1/40 N hydrochloric acid was added to the hydrolyzate, and the excess of the latter was back titrated.

32.8 mg substance: 6.12 ml 1/40 N NaOH. 22.1 mg substance: 4.10 ml 1/40 N NaOH. $C_{23}H_{26}O_6N_2$.
Calculated: 6.11 ml 1/40 N NaOH. 4.10 ml 1/40 N NaOH.

Reaction of N-Benzoylserine with 2-phenyl-4-benzyl-5-oxazolone

2-Phenyl-4-benzyl-5-oxazolone was prepared from benzoylphenylalanine and acetic anhydride. M.p. 69°. 1 g of N-benzoylserine in dioxane was mixed with a solution of 1.5 g of oxazolone in chloroform. The mixture was heated for 6 hours to gentle boiling. The chloroform and dioxane were removed in vacuum, and the residual oil was dissolved in absolute benzene. Upon standing, crystals of N-benzoylserine (0.87 g) precipitated slowly. A mixed sample with an N-benzoylserine preparation did not give a depression in melting point. Therefore, the reaction between benzoylserine and 2-phenyl-4-benzyl-5-oxazolone did not occur.

Synthesis of O-(Benzoylphenylalanyl)-N-benzoylserine (III)

A solution of 3.0 g of benzoylserine in dioxane was added to a chloroform solution of the acid chloride obtained from 4.0 g of benzoylphenylalanine. The mixture was boiled for 6 hours, concentrated in vacuum, and the residual oil dissolved in absolute benzene. Crystals precipitated upon standing; they were filtered and washed with benzene, ether, and water. O-Benzoylphenylalanyl)-N-benzoylserine was recrystallized from a mixture of dichloroethane and alcohol. M.p. 171°. Yield 2.0 g. The substance was soluble in alcohol, acetone, hot dichloroethane and insoluble in water, benzene, and toluene.

The compound has not been reported in the literature.

Found %: C 67.23, 67.47; H 5.38, 5.31; N 6.09, 5.98. $C_{26}H_{24}O_6N_2$. Calculated %: C 67.82; H 5.22; N 6.08.

Preparation of the Isopropyl Ester of N,O-Di(phthalylglycyl)-serine (V)

1.38 g of serine isopropyl ester hydrochloride and 3.6 g of phthalylglycyl acid chloride were heated to 100-105° (glycerine bath) in 10 ml of dioxane until the evolution of hydrogen chloride ceased, and for 10 minutes more. The dioxane was distilled off in vacuum. The residue, a dark, tarry mass, was dissolved with heating in 6 ml of dioxane. 8 ml of ligroin was added to the solution. After strong shaking, crystallization started. 10 ml more of ligroin was added to the solution, the residue was filtered, washed with petroleum ether, and recrystallized from a mixture of alcohol and dioxane (1:1). 2.7 g of the isopropyl ester of N,O-di-(phthalylglycyl)serine was obtained. Yield 69% of the theoretical. M.p. 170-171°. The substance crystallized in the form of very thin needles; it was soluble in dioxane and dichloroethane, difficultly soluble in alcohol, and insoluble in water and ligroin.

The compound has not been reported in the literature.

Found %: C 59.67, 59.48; H 4.70, 4.64; N 8.15, 8.20. $C_{26}H_{23}O_9N_3$. Calculated %: C 59.88, H 4.41; N 8.06.

Preparation of the Methylamide of O-(benzoylphenylalanyl)-N-benzoylserine (VI)

a) Preparation of the methylamide of N-benzoylserine. 5 g of N-benzoylserine was esterified with methyl alcohol under the usual conditions for the esterification of amino acids and their derivatives. The oil remaining after the removal of the methyl alcohol and hydrogen chloride was treated with an ether solution of methylamine, and allowed to stand for two days. The ether was removed in vacuum, and the residual oil crystallized upon standing. After recrystallization from absolute alcohol, the methylamide of N-benzoylserine was obtained in the form of long, white needles, readily soluble in water, aqueous alcohol, with heating in dioxane, absolute alcohol, and methyl ethyl ketone. M.p. 146.5°. Yield 3.5 g, 65 % of the theoretical.

The compound has not been reported in the literature.

Found %: C 59.60, 59.70; H 6.35, 6.45; N 12.55, 12.68. $C_{11}H_{14}O_3N_2$. Calculated %: C 59.45; H 6.30; N 12.61.

b) Preparation of the methylamide of O-(benzoylphenylalanyl)-N-benzoylserine. 0.5 g of the methylamide of N-benzoylserine, dissolved in dioxane, was added to a chloroform solution of benzoylphenylalanyl acid chloride obtained from 1 g of benzoylphenylalanine. The mixture was heated for 4 hours at 50-60° and allowed to stand overnight. The oil remaining after the removal of the solvents was treated with absolute benzene. Upon standing, crystals formed, which were washed many times with benzene, sodium carbonate solution, and water. The substance was recrystallized from alcohol and dried in vacuum at 80° over phosphoric anhydride. M.p. 181°. Yield 0.8 g, 77% of the theoretical.

The compound has not been reported in the literature.

Found %: C 67.93, 67.87; H 5.98, 5.85; N 8.62, 8.78. $C_{27}H_{27}O_5N_3$. Calculated %: C 68.49; H 5.71; N 8.88.

SUMMARY

Methods for the synthesis of O,N-peptides of serine were studied. The following peptides were prepared: O-(benzoylphenylalanyl)-N-benzoylserine, the ethyl ester of O-(benzoylaminoisobutyryl)-N-benzoylserine, the isopropyl ester of N,O-di-(phthalylglycyl)serine, and the methylamide of O-(benzoylphenylalanyl)-N-benzoylserine.

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* See Consultants Bureau English translation, page 1675.

** See Consultants Bureau English translation, page 1101.

REACTION OF HYDROGEN SULFIDE WITH OXIDES OF THE ACETYLENIC AND VINYLACETYLENIC SERIES

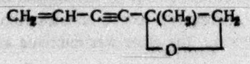
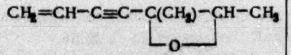
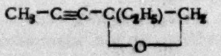
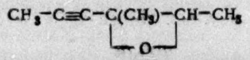
I. SYNTHESIS OF VINYL AND ALKYL THIOPHENES

F. Ya. Perveev and N. I. Kudryashova

By the reaction of hydrogen sulfide with ethylene oxides, hydroxyethylmercaptans or dithioglycols are formed in relation to the temperature conditions and the ratio of the reagents [1]. Thioglycerines are obtained from glycide oxides and hydrogen sulfide in the form of two isomers [2]. By passing a mixture of hydrogen sulfide and ethylene oxide over Al_2O_3 at 350-400°, thiophene, 2,5-dimethylthiophene, and other higher homologs of thiophene, as well as the lower mercaptans are formed [3]; at 200-250°, thioxane and dithiane [4].

The reaction of hydrogen sulfide with the following oxides, whose formulas and constants are given in the Table, was studied: 2-methylepoxy-1,2-hexen-5-yne-3 (I), 3-methylepoxy-2,3-hepten-6-yne-4 (II), 2-ethylepoxy-1,2-pentyne-3 (III), and 3-methylepoxy-2,3-hexyne-4 (IV).

A colorless, readily volatile liquid with a specific odor was obtained by the reaction of oxide (I) with hydrogen sulfide. An acid of composition $C_6H_6O_2S$, melting at 120-121° (β'-methyl-α-thiophene carboxylic acid) was obtained by the oxidation of this substance and its hydrogenation product with potassium permanganate. The structure α-vinyl-β'-methylthiophene could be assigned to the product synthesized on the basis of the data obtained. The fact that the constants of the substance obtained coincided with those of the compound synthesized by another method [5] served as a confirmation of the above conclusion.

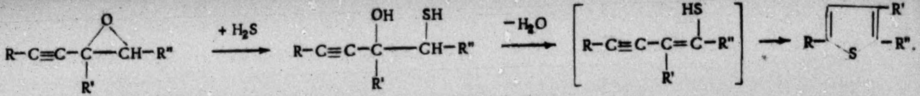
No.	Formula	Melting point	d_4^{20}	n_D^{20}
(I)	 $CH_2{=}CH{-}C{\equiv}C{-}C(CH_3){-}CH_2$ (epoxide, –O–)	50-51° (15 mm)	0.9249	n_α^{20} 1.4739
(II)	 $CH_2{=}CH{-}C{\equiv}C{-}C(CH_3){-}CH{-}CH_3$ (epoxide, –O–)	54-55° (12 mm)	0.9005	1.4881
(III)	 $CH_3{-}C{\equiv}C{-}C(C_2H_5){-}CH_2$ (epoxide, –O–)	40-41° (8 mm)	0.8966	1.4436
(IV)	 $CH_3{-}C{\equiv}C{-}C(CH_3){-}CH{-}CH_3$ (epoxide, –O–)	59-60° (28 mm)	0.8856	1.4410

α-Vinyl-α',β'-dimethylthiophene was obtained by the action of hydrogen sulfide on oxide (II), and α-methyl-β'-ethylthiophene, from oxide (III). The physical constants of α-methyl-β'-ethylthiophene, previously reported in the literature [6] coincide with those of the substance obtained. α,α',β'-Trimethylthiophene is formed by the reaction of hydrogen sulfide with oxide (IV). It is an easily volatile colorless liquid with a specific odor which is soluble in strong sulfuric acid, gives a characteristic indophenone color with isatin sulfate, and forms a white crystalline precipitate with mercury acetate.

Based on the above results, it can be considered established that the reaction of hydrogen sulfide with oxides of the acetylenic and vinylacetylenic series is a general one for the synthesis of vinyl and alkylthiophenes.

Up to now alkyl thiophenes have been prepared by the treatment with phosphorous pentasulfide of γ-keto acids [7], γ-dicarboxylic acids [8], 1,4 diketones [9], or from furane derivatives by the action of hydrogen sulfide at high temperatures in the presence of a catalyst [10], and others. Vinyl thiophenes were prepared by the reduction of acetylthiophenes to the corresponding alcohols and their subsequent dehydration [11, 12, 13], and by the reaction of thienyl magnesium bromide with vinyl chloride in the presence of $CoCl_2$ [14].

The formation of vinyl and alkylthiophene from oxides of the acetylenic and vinylacetylenic series by the reaction with hydrogen sulfide, evidently, occurs according to the following scheme:



The rate of formation of the thiophene derivatives depends on the temperature conditions of the reaction, and the structural peculiarities of the oxides. Disubstituted oxides of type (III) react with hydrogen sulfide considerably more rapidly than the trisubstituted of type (IV). In addition, radicals which substitute for the acetylenic hydrogen have a considerable effect on the reactivity of the oxide ring. Thus, for example, 2-methylepoxy-1,2-hexen-5-yne-3 (I) reacts with hydrogen sulfide at room temperature with a great evolution of heat, while heating for several hours is necessary for the preparation of α-vinyl-α',β'-dimethylthiophene from 3-methylepoxy-2,3-hepten-6-yne-4 (II).

EXPERIMENTAL

1. Preparation of α-Vinyl-β'-methylthiophene

20 g of $Ba(OH)_2$ and 150 ml of water were placed into a round bottomed flask with a mechanical stirrer, and a stream of hydrogen sulfide was passed in with intensive stirring with a simultaneous addition of 30 g of oxide (I). The addition of the oxide was regulated in such a manner that the temperature of the reaction mixture did not go above 50°. After the addition of the oxide, the hydrogen sulfide was passed in for one hour more. The reaction mixture was then acidified with the calculated amount of acetic acid. The reaction products were extracted with ether, the ether layer was dried, the ether was removed, and after 2 distillations, the substance was obtained in the form of a colorless liquid with b.p. 67-70° at 10 mm, n_D^{20} 1.5580, d_4^{20} 1.0110. It gradually polymerized upon storage in the air to form a viscous mass. Yield 25 g, 73-75% of the theoretical. It dissolved in strong sulfuric acid, gave a characteristic indophenone reaction with isatin. It formed a crystalline precipitate with mercury acetate.

0.4539 g substance: 0.8470 g $BaSO_4$. Found %: S 25.63. C_7H_8S. Calculated %: S 25.80.

Hydrogenation of α-vinyl-β'-methylthiophene. The hydrogenation was effected over Raney Ni in ether solution. 1158 ml of hydrogen (22°, 764 mm) was consumed for the hydrogenation of 6 g of the substance; 1085 ml of H_2 was required based on one double bond. The hydrogenation product was first dried with $CaCl_2$ and then with metallic sodium, and it was distilled over Na; b.p. 158-159°, n_D^{20} 1.5061; d_4^{20} 0.9652.

Oxidation of α-vinyl-β'-methylthiophene. 22.4 g of $KMnO_4$ was used for the oxidation of 6.28 g of the substance. The oxidation was conducted in alkaline medium (3 g of NaOH in 800 ml of water). No neutral substances and volatile acids with the exception of an acid of the composition $C_6H_6O_2S$, which was extracted with ether from the acidified aqueous solutions, could be detected among the oxidation products. The ether was removed and the substance obtained was recrystallized from water; m.p. 120-121°.

0.3208 g substance: 0.5236 g $BaSO_4$. Found %: S 22.41. $C_6H_6O_2S$. Calculated %: S 22.55.

Oxidation of the hydrogenation product of α-vinyl-β'-methylthiophene. 24.4 g of $KMnO_4$ was used for the oxidation of 4.7 g of the substance. The oxidation was conducted in alkaline medium. An acid was isolated from among the products, which melted at 120-121° and did not give a depression in melting point when mixed with the previously isolated product.

2. Preparation of α-Vinyl-α',β'-dimethylthiophene.

30 g of 3-methylepoxy-2,3-hepten-6-yne-4 (II), 20 g of $Ba(OH)_2$ and 150 ml of water were used. The hydrogen sulfide was passed into the reaction mixture for 8 hours at 60-70°.

17 g of a substance with b.p. 68-70° at 8 mm was isolated; n_D^{20} 1.5545, d_4^{20} 0.9938; MR_D 44.6. $C_8H_{10}S\lceil_3$. Calculated 43.47.

The substance obtained was a colorless, mobile liquid, with a characteristic odor. Upon storage in the air, it yellowed. It formed a white precipitate with mercury acetate which decomposed at 250°. It gave a dark, wine-red coloration with isatin and strong sulfuric acid. Yield 50% of the theoretical.

0.3846 g substance: 0.6438 g $BaSO_4$. Found %: S 22.99. $C_8H_{10}S$. Calculated %: S 23.20.

If the synthesis was effected at 80-90°, the reaction was completed in 2 hours, and the yield of the product was somewhat increased. In the first, as well as in the second synthesis, the formation of tarry products occurred, evidently, because of the polymerization of the oxide.

3. Preparation of α-methyl-β'-ethylthiophene

2-Ethyl-1-chloropentyne-3-ol-2. 30 liters of methylacetylene was passed in over a 12-hour period into an ether solution of 1 mole of ethyl magnesium bromide. Then 15 g of 1-chlorobutanone-2 was added with stirring and cooling (water and ice). The reaction mixture was left to stand overnight. The organo-magnesium complex was decomposed with 30% acetic acid. The ether layer was separated, the water was extracted with ether, dried with Na_2SO_4, and the ether was removed. The substance obtained had the following constants after 2 distillations: b.p. 75-77° at 8 mm, n_D^{20} 1.4711, d_4^{20} 1.0571; MR_D 38.8. $C_7H_{11}OCl\models$ Calculated 38.92.

0.2483 g substance: 0.2436 g AgCl. 0.1135 g substance: 18.7 ml CH_4 (16.5°, 767.4 mm). Found %: Cl 24.27; Active H 0.695. $C_7H_{11}OCl$. Calculated %: Cl 24.18; active H 0.688.

2-Ethylepoxy-1,2-pentyne-3 (III). Oxide (III) was isolated upon the treatment of the chlorohydrin with powdered KOH in ether solution and was a colorless liquid with b.p. 40-41° at 8 mm, n_D^{20} 1.4436, d_4^{20} 0.8966; MR_D 32.9. $C_7H_{10}O\models$. Calculated 32.8.

0.1164, 0.1282 g substance: 0.3248, 0.3574 g CO_2; 0.0969, 0.1055 g H_2O. Found %: C 76.15, 76.08; H 9.32, 9.21. $C_7H_{10}O$. Calculated %: C 76.32; H 9.15.

α-Methyl-β'-ethylthiophene. 100 ml of water, 15 g of $Ba(OH)_2$, and 25 g of oxide (III) were placed in a round-bottomed flask with a mechanical stirrer and a reflux condenser. Hydrogen sulfide was passed in for 15 hours at 50-60°. The processing of the reaction mixture was effected by the above reported method. The product obtained was dried with $MgSO_4$ and vacuum distilled at 50-51° (10 mm); 15 g of methylethylthiophene was isolated and 4 g of the oxide (III) was recovered. Methylethylthiophene was dried and distilled over metallic sodium at 161-162°; d_4^{20} 0.9710, n_D^{20} 1.5070; MR_D 38.69. $C_7H_{10}S\models_2$. Calculated 39.31.

The substance dissolved in sulfuric acid and gave a characteristic violet coloration with isatin sulfate and formed a crystalline compound with mercury acetate.

0.1984, 0.1715 g substance: 0.3648, 0.3146 g $BaSO_4$. Found %: S 25.25, 25.19. $C_7H_{10}S$. Calculated %: S 25.41.

Oxidation of methylethylthiophene. 3 g of the substance, 15.5 g of $KMnO_4$ (calculated for the oxidation of the ethyl group) 1.5 g of NaOH, and 500 ml of water were used. The $KMnO_4$ was added gradually in small portions, the oxidation was continued for 8 hours at ordinary temperatures. Neutral products were not detected. An acid with m.p. 97-99° was isolated by extraction of the acidified aqueous solution.

4. Preparation of α,α',β'-Trimethylthiophene

3-Methyl-2-chlorohexyne-4-ol-3. The chlorohydrin was prepared by the above method. 80 g of 2-chlorobutanone-3 was used for 1 mole of methylacetylenyl magnesium bromide. 72 g of the substance (65% of theory) with b.p. 66-67.5° at 7 mm, n_D^{15} 1.4671. d_4^{15} 1.0535; MR_D 38.62. $C_7H_{11}OCl\models$. Calculated 38.92.

0.2817 g substance: 0.2745 g AgCl. Found %: Cl 24.10. $C_7H_{11}OCl$. Calculated %: Cl 24.18.

3-Methylepoxy-2,3-hexyne-4 (IV). A substance with b.p. 43-44° at 12 mm was isolated by the treatment of the chlorohydrin with powdered KOH in ether solution; MR_D 32.84. $C_7H_{10}O\models$. Calculated 32.80.

0.1239, 0.1200 g substance: 0.3468, 0.3350 g CO_2; 0.1029, 0.1003 g H_2O. Found %: C 76.27, 76.18; H 9.29, 9.35. $C_7H_{10}O$. Calculated %: C 76.32; H 9.15.

α,α',β'-Trimethylthiophene. 100 ml of water, 15 g of $Ba(OH)_2$, 20 g of oxide (IV) were placed into a round bottomed flask with a mechanical stirrer. Hydrogen sulfide was passed in at a reaction mixture temperature of 50-60° for 10 hours. After the corresponding processing of the reaction mixture, the synthesized substance was distilled over metallic sodium. 8 g was isolated with b.p. 162-163°; n_D^{20} 1.5104, d_4^{20} 0.9730; MR_D 38.82. $C_7H_{10}S\models_2$. Calculated 39.31

0.2125, 0.1988 g substance: 38.5 ml NaOH (T = 0.003747); 38.0 ml NaOH (T = 0.003275). Found %: S 25.4, 25.1. $C_7H_{10}S$. Calculated %: S 25.41.

In addition to trimethylthiophene, 10 g of the starting oxide was isolated during the distillation of the product obtained. The yield of trimethylthiophene was 73% of the theoretical based on the reacted oxide. At 80-90° the reaction proceeded to completion and is completed within a shorter time.

SUMMARY

1. A general method was developed for the preparation of vinyl and alkylthiophenes by the reaction of

oxides of the acetylenic and vinylacetylenic series with hydrogen sulfide in the presence of $Ba(OH)_2$.

2. α-Vinyl-β'-methylthiophene, α-vinyl-α',β'-dimethylthiophene, α-methyl-β'-ethylthiophene, and α,α',β'-trimethylthiophene were synthesized with this method.

3. A probable scheme for the formation of vinyl and alkylthiophenes was proposed.

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SYNTHESIS BASED ON ANABASINE

VI. AMINATION OF ANABASINE, N-METHYLANABASINE, AND NICOTINE

A. Sadykov, O. Otroshchenko, and M. Yusupov

The previous investigation [1] was concerned with the study of the transformation products of N-(β-hydroxyethyl)anabasine. The present communication reports the results of the study of the amination reaction of anabasine, N-methylanabasine, and nicotine without solvents. The amination of anabasine and its derivatives with alkali metal amides in various solvents [2, 3, 4] showed that better yields of the reaction products were obtained by using dimethylanaline. In view of the fact that dialkyl amines are not always readily available solvents, and that A. Chichibabin [5] showed with pyridine that amination can occur by the direct reaction of the reagents, it was of interest to conduct this reaction with anabasine, N-methylanabasine, and nicotine. The main subject of this study of the amination reaction was anabasine.

The starting substances were prepared in the following manner: anabasine was separated from a low boiling fraction of anabasine sulfate by the hydrochloride method [6]; N-methylanabasine was preparedby reacting anabasine with formaldehyde and formic acid by the method of Orekhov and Norkina [7]. Nicotine was separated from nicotine sulfate by the usual method. The bases obtained were characterized by physical constants and by the preparation of characteristic salts. A ratio of base to sodium amide of 1 mole to 2 moles with a small excess of the latter. The amination of anabasine was effected by heating a mixture of the reacting substances under the usual conditions and under pressure for 12 hours at various temperatures.

α'-Aminoanabasine could be obtained in a yield of 22.2% by effecting the reaction under pressure (in an autoclave) at 150-160°. Further increasing the temperature leads to a strong tarring of the reaction products. The amination of anabasine under the usual conditions (without an autoclave) also gave α'-aminoanabasine with a yield of 6.80%. In both cases, noticeable amounts of α-aminoanabasine could not be isolated, which were always formed during the amination of anabasine in a solvent (see the Table). Increasing the reaction time, did not effect the yield of the products of the amination to any great extent under ordinary conditions, as well as under pressure.

Expt. No.	Reagents (in g)		Heating temperature	Yield of aminoanabasine	
	Anabasine	Sodium amide		(in g)	(in % of theoretical)
1	10.0	5.76	100°	–	–
2	20.0	11.50	130 - 140	0.56	2.57
3	13.4	8.62	140 - 150	1.40	9.58
4	20.0	11.50	150 - 160	4.85	22.2
5	15.5	8.78	160 - 180	1.16	6.84
6	20.0	11.50	180 - 200	1.39	6.43

The amination of nicotine was effected at 150-160° (in an autoclave) as with anabasine, and α'-aminonicotine was obtained in a yield of 87.9%. It must be mentioned that the yield of α'-aminonicotine considerably exceeded that total yield of aminonicotines obtained by the amination of nicotine in xylene as a solvent [8].

The amination of N-methylanabasine was effected by heating a mixture of the reacting substances at 140-155° for 12 hours. In contrast to anabasine and nicotine, two isomers were obtained as a result of the reaction: α-amino-N-methylanabasine in a yield of 23.3% and α'-amino-N-methylanabasine in a yield of 37.7%. The total yield of the N-methylaminoanabasines, 61.0%, does not differ from the total yield of the products of the amination in dimethylaniline [9]. The reaction, effected under the above conditions but under pressure made it possible to obtain a total yield of aminoderivatives of 70.6%.

Therefore, considerably better results were obtained by the amination of nicotine and N-methylanabasine with sodium amide in an autoclave in comparison to those obtained by effecting the reaction in solvents (without an autoclave). This can be explained by the presence of a methyl group on the nitrogen of these bases which increases the activity of the α and α' hydrogen atoms in the pyridine nucleus, especially the α'-hydrogen atom, since considerably more of α'-aminoderivative is obtained. On the other hand, nicotine and N-methylanabasine are less prone to tarring than anabasine.

EXPERIMENTAL

1. Separation of anabasine from a mixture of anabasine and lupinine. 390 g of a mixture of anabasine and lupinine (containing 88.4% of anabasine) was dissolved in 1000 ml of acetone. 77.5 g of hydrogen chloride in acetone was added in small portions with cooling and stirring to the solution. The precipitation of anabasine hydrochloride started. The reaction mass was allowed to stand until the following day. The precipitate was filtered, washed many times with acetone, and recrystallized from a mixture of alcohol and acetone. For the preparation of the base, the hydrochloride was dissolved in a small volume of water and treated with a 40% solution of potassium hydroxide until a weakly basic reaction occurred. The oil which precipitated was extracted with benzene. The benzene solution was dried over fused sodium sulfate and the solvent removed. The residue was vacuum distilled at 139-142° (14 mm). Yield 313.7 g (91% of the theoretical).

2. Amination of anabasine (in an autoclave) (typical experiment). A mixture of 20 g of anabasine (1 mole) and 11.5 g of sodium amide (2.4 moles) was heated in an autoclave for 12 hours at 150-160°. The reaction product which was a solid dark mass, was decomposed (with cooling) with a small amount of water. The solution obtained was saturated with sodium carbonate and extracted many times with ether. The ether extracts were combined and dried with fused potassium carbonate. After the removal of the solvent, the residue was vacuum distilled.

The following fractions were obtained: Fraction 1: 137-139° (10 mm), 3.46 g, unchanged anabasine; fraction 2: 165-190° (10 mm) 4.85 g (yield 22.2 %), α'-aminoanabasine.

The second fraction was dissolved in hot toluene. Upon standing, crystalline α'-aminoanabasine precipitated from the solution. Recrystallized from toluene, α'-aminoanabasine had an m.p. of 109°. α'-Aminoanabasine was readily soluble in water and alcohol, difficultly in ether, and benzene. The picrate had an m.p. of 231-233°. A mixed melting point determination with α'-aminoanabasine picrate prepared by the amination of anabasine in dimethylaniline did not give a depression.

3. Amination of anabasine. 20 g of anabasine (1 mole) and 11.5 g of sodium amide (2.4 moles) were heated for 12 hours. The subsequent processing was as in the previous experiment. The residue was vacuum distilled, and the following fractions were obtained: fraction 1, 135-140° (10 mm), 6.5 g, unchanged anabasine; fraction 2, 165-180° (10 mm), 1.48 g (6.8%), α'-aminoanabasine.

Crystalline α'-aminoanabasine was obtained by solution in toluene. After recrystallization from hot toluene, the m.p. was 108-109°. α'-Aminoanabasine picrate had an m.p. of 231-233°.

4. Amination of nicotine. A mixture of 30 g of nicotine (1 mole) and 17.28 g (2.4 moles) of sodium amide was heated in an autoclave for 12 hours at 150-160°. The reaction product was processed in the usual manner. After distillation in vacuum, a fraction boiling at 164-170° (0.5 mm), 28.6 g (87.7%) was obtained. The constants corresponded with the literature data for α'-aminonicotine [9].

The hydrochloride. Concentrated hydrochloric acid was added dropwise to the α'-aminonicotine until an acid reaction appeared on Congo. The solution obtained was evaporated to dryness on the water bath. The crystalline residue had an m.p. 136-138° after two recrystallizations from alcohol.

5. Amination of N-methylanabasine. 30 g (1 mole) of N-methylanabasine and 16.6 g (2.4 moles) of sodium amide were heated in an autoclave at 150-160° for 12 hours. The reaction mixture was decomposed with water, saturated with sodium carbonate, and exhaustively extracted with ether. The combined ether extracts were dried over fused potassium carbonate. The residue, after the removal of the solvent, was vacuum distilled. The following fractions were obtained: fraction 1: 155-160° (7 mm), 7.6 g (yield 23.3 %), α-amino-N-methylanabasine; fraction 2: 162-167° (7 mm), 12.3 g (yield 37.7 %), α'-amino-N-methylanabasine. α-Amino-N-methylanabasine picrate (from alcohol) had an m.p. 234-235°. α'-Amino-N-methylanabasine picrate (from water) had an m.p. 216-217°.

6. Amination of N-methylanabasine. A mixture of 30 g (1 mole), of N-methylanabasine and 21.5 g (2.9 moles) of sodium amide were heated in an autoclave at 150-160° for 12 hours. The cooled mass was decomposed with water and extracted with benzene. The benzene solution was dried over fused potassium carbonate; the solvent was removed, and the residue subjected to vacuum distillation (at 13 mm).

Fraction 1: b.p. 155-160° (7 mm), α-amino-N-methylanabasine, 8 g (yield 24.5 %); fraction 2: 162-167° (7 mm), α'-amino-N-methylanabasine, 15.0 g (yield 46.1%). α -Amino-N-methylanabasine picrate melted at 233-235°. α'-Amino-N-methylanabasine picrate meltes at 216-219.

SUMMARY

1. It was shown that the amination reaction of anabasine, nicotine, and N-methylanabasine with sodium amide can occur without solvents; the α'-isomer was obtained preferentially by the amination of anabasine and nicotine. Upon the amination of N-methylanabasine, a mixture of two isomeric amino-N-methylanabasine was obtained with the α'-isomer predominating.

2. The total yield of the amination products of anabasine, N-methylanabasine, and nicotine in an autoclave without a solvent was greater than when the reaction was conducted in dialkylamine solutions.

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* See Consultants Bureau English translation, page 1007.

SYNTHESIS OF β-PHENYL-β-(N-METHYLAMINO)PROPIONIC ACID AND SEVERAL OF ITS DERIVATIVES

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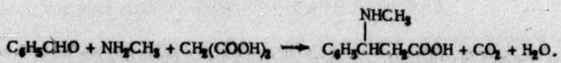
The problem of the present investigation was the preparation of N-alkyl-β-amino acids in order to compare their properties and transformations with β-amino acids with primary amino groups. β-Phenyl-β-(N-methylamino)-propionic acid was prepared initially.

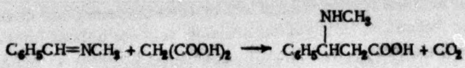
This compound was first synthesized by Rodionov and Zenkovich by the reaction between benzaldehyde, malonic acid, and an alcoholic methylamine solution.



$$C_6H_5CHO + NH_2CH_3 + CH_2(COOH)_2 \longrightarrow C_6H_5\overset{\overset{NHCH_3}{|}}{C}HCH_2COOH + CO_2 + H_2O.$$

The main product in addition to the methylamino acid was cinnamic acid.

Somewhat later phenylmethylaminopropionic acid was obtained by Johnson [1] in greater yield, who synthesized this compound by condensation of benzalmethylamine with malonic acid in an absolute alcoholic medium.



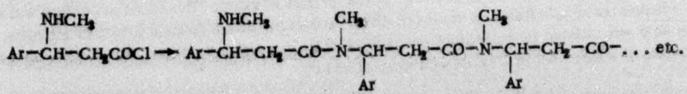
$$C_6H_5CH{=}NCH_3 + CH_2(COOH)_2 \longrightarrow C_6H_5\overset{\overset{NHCH_3}{|}}{C}HCH_2COOH + CO_2$$

The yield of the N-methylamino acid by this method was 40% of the theoretical based on the benzal derivative. Cinnamic acid was also formed. Yield, 38% of the theoretical.

It was shown by the authors that, if the condensation of benzalmethylamine with malonic acid was effected in a benzene medium, an increase of the yield of the methylamino acid to 50-55% and a decrease in the formation of cinnamic acid to 27-33% occurred.

It was decided to prepare as the initial derivative of N-methyl-β-phenyl-β-alanine, N-methylphenylglyoxalidone by the Hoffman reaction. N-methyl-β-phenyl-β-alanyl chloride, necessary for the preparation of the amide, was prepared by the action of thionyl chloride on N-methyl-β-phenyl-β-alanine and was isolated as the hydrochloride in a good yield.

A series of difficulties were encountered during the preparation of N-methyl-β-phenyl-β-alanyl amide. During attempts to amidate the acid chloride with dry ammonia, the formation of high molecular compounds occurred arising, evidently, as a result of the intermolecular condensation of the acid chloride with an N-methyl group of a second molecule.



$$Ar{-}\overset{\overset{NHCH_3}{|}}{C}H{-}CH_2COCl \longrightarrow Ar{-}\overset{\overset{NHCH_3}{|}}{C}H{-}CH_2{-}CO{-}\overset{\overset{CH_3}{|}}{N}{-}\underset{\underset{Ar}{|}}{C}H{-}CH_2{-}CO{-}\overset{\overset{CH_3}{|}}{N}{-}\underset{\underset{Ar}{|}}{C}H{-}CH_2{-}CO{-}\ldots \text{etc.}$$

The preparation of the ester of the amino acid was accompanied by deamination; a mixture of the esters of cinnamic and β-phenyl-β-(N-methylamino)propionic acids resulted. As a result, the ester of the amino acid was isolated in the form of the hydrochloride and in low yield. In subsequent experiments, the reaction for the preparation of the amide was conducted without the isolation of the ester in the free state by the action of ammonia in the cold on a solution of the acid chloride in alcohol. The reaction mixture obtained was usually allowed to stand for 10-12 days at room temperature, and the desired amide was isolated in a yield of 25-30% of the theoretical.

The ease of the process of deamination of the amide of N-methyl-β-phenyl-β-alanine, as well as the possible action of hypobromite on the unprotected secondary amino group complicated the course of the Hoffmann reaction, and for this reason, N-methylphenylglyoxalidone was only prepared in a low yield (20-25%). Tests conducted at the Microbiological Institute of the Academy of Sciences of the U.S.S.R. showed that the glyoxalidone did not possess antibiotic activity.

For the further characterization of β-phenyl-β-(N-methylamino)propionic acid, its N-nitroso-N-benzoyl derivative and its amide were synthesized in good yields.

During attempts to cyclize N-benzoyl-N-methyl-β-phenyl-β-alanylamide into 1-methyl-2,6-diphenyl-4-oxo-tetrahydropyrimidine by the action of acetic anhydride, a thick oil was isolated which did not distill at ordinary or reduced pressures. The reaction product did not lend itself for purification by means of crystallization from various organic solvents either. N-benzoyl-N-methyl-β-phenyl-β-alanine was isolated in unchanged form from the mother liquor without contamination with benzoic acid. The absence of the last compound showed that reaction of N-benzoyl-N-methyl-β-phenyl-β-alanylamide with acetic anhydride was not accompanied by trans-acylation, in contrast to amino acids with primary amino groups [2].

The dehydration of the amide did not occur even upon heating with oxalic acid in benzene and toluene. Upon heating N-benzoyl-N-methyl-β-phenyl-β-alanylamide with oxalic acid without solvents, the reaction started at 145-150°. It was shown that the main product of the reaction was cinnamic amide which formed as a result of the deamination process of the amide, and that the formation of the tetrahydropyrimidine ring did not occur.

EXPERIMENTAL

Synthesis of N-methyl-β-phenyl-β-alanine. A mixture of 28.5 g of benzalmethylamine, 23 g of malonic acid, and 115 ml of benzene was heated to boiling on the water bath for 8 hours. The evolution of carbon dioxide gas and the formation of a precipitate of the aminoacid occurred. At the end of the reaction, ether was added to the cooled reaction mixture for the complete precipitation of the amino acid (the ether and benzene used in this experiment were dried over calcium chloride).

The precipitated amino acid was filtered, washed with ether on the funnel, and dried. M.p. 167-168°, yield 20.8 g, i.e., 52.5% of the theoretical. 11.2 g of the cinnamic acid was isolated from the ether benzene filtrate which was 34.2% of the theoretical.

Preparation of β-phenyl-β-(N-methylamino)propionylacid chloride. 10 g N-methyl-β-phenyl-β-alanine was added gradually to 22 g of thionyl chloride with ice cooling. The mixture obtained was heated on the water bath for 2 hours at 45-50° (thermometer inside the flask). The precipitated light yellow residue which was the hydrochloride of N-methyl-β-phenyl-β-alanine, was filtered, washed with benzene, then ether, and dried in a vacuum desiccator. Yield 11.2 g of white crystals, (about 85.7 % of the theoretical). The substance melted at 128-129° (with decomposition).

Found %: Cl 30.10, 29.92; N 6.12. $C_{10}H_{13}ONCl_2$. Calculated %: Cl 30.34; N 5.98.

Synthesis of the ester of N-methyl-β-phenyl-β-alanine. 2 g of N-methyl-β-phenyl-β-alanine, 10 ml of absolute alcohol, and 2 g of concentrated sulfuric acid were heated to boiling on a water bath for 5 hours. At the end of the reaction, the alcohol was removed, and the solution was extracted with ether after neutralization with sodium hydroxide. The oil remaining after the removal of the ether did not give a definite boiling point at ordinary, as well as reduced pressures. The odor of methylamine was detected upon distillation. Evidently, the process of deamination occurred, and the ether ester of N-methyl-β-phenyl-β-alanine was partially converted into ethyl cinnamate. This assumption was proved by the analysis for nitrogen of the mixture of esters. The nitrogen content was equal to 3.7 and 3.9 %, whereas the ethyl ester of N-methyl-β-phenyl-β-alanine should contain 6.76 % of nitrogen. The ester of the amino acid was isolated in the form of the hydrochloride by passing hydrogen chloride into an ether solution of the mixture of esters. White crystals with m.p. 113-114°.

Found %: N 5.91, 6.12. $C_{12}H_{17}O_2N \cdot HCl$. Calculated %: N 5.75.

Synthesis of N-methyl-β-phenyl-β-alanylamide. 10 g of N-methyl-β-phenyl-β-alanyl acid chloride hydrochloride was dissolved in 100 ml of absolute alcohol, saturated with ammonia in the cold, and left in a closed container for 8-10 days at room temperature. The precipitated ammonium chloride was filtered, and the alcohol was removed. The residue after the removal of the alcohol was a mixture of crystals, soluble in a sufficient amount of water, and an oil insoluble in water and hydrochloric acid. After treating the residue with water, the oil which separated was extracted with ether, and after the removal of the ether and rectification, 4 g of ethyl cinnamate was obtained.

The remaining aqueous solution was evaporated to a small volume. The separated crystals of N-methyl-β-phenyl-β-alanylamide hydrochloride were recrystallized from ethyl alcohol. 2.5 g white needles with m.p. 215-216° was obtained. The yield of the amide hydrochloride was 26.7 %, and about 58% of the theoretical based on the acid chloride not subjected to the deamination process.

Found %: N 13.24, 13.27. $C_{10}H_{15}ON_2Cl$. Calculated %: N 13.05.

The base of N-methyl-β-phenyl-β-alanyl amide was very soluble in H_2O. In order to isolate it, an aqueous solution of the hydrochloride was neutralized with sodium carbonate, evaporated to dryness, and extracted with absolute alcohol. After the removal of the alcohol, the compound obtained was recrystallized from benzene. White crystals with m.p. 103-104°.

Found %: N 15.75, 15.76. $C_{10}H_{14}ON_2$. Calculated %: N 15.72.

Synthesis of N-methylphenylglyoxalidone. 2 g of bromine was added dropwise to a solution of 4 g of potassium hydroxide in 20 ml of water cooled to −8-10°. 1.6 g of N-methyl-β-phenyl-β-alanylamide hydrochloride was added gradually to the obtained solution of the hypobromite at the same temperature. After 2 hours, the clear yellow solution obtained was slowly heated to 80°. At about 55°, the liquid in the flask clouded as a result of the separation of the intermediate compound in the form of an oil. Upon further increase in temperature, the liquid once more became transparent. The heating was continued for 10 minutes at 80°. Upon cooling, yellow crystals of N-methylphenylglyoxalidone slowly precipitated from the solution in an 0.3 g quantity (22.9% of the theoretical). Its melting point was 147-148°, and after recrystallization from water with carbon or from alcohol, white needles with m.p. 150-151° were obtained.

Found %: C 67.98, 68.08; H 6.74, 6.82; N 16.14. $C_{10}H_{12}ON_2$. Calculated %: C 68.16; H 6.81; N 15.90.

Synthesis of N-nitroso-N-methyl-β-phenyl-β-alanine. A solution of 2 g of sodium nitrite in 20 ml of water was added to a solution of 4 g of the N-methylamino acid in 40 ml of 5% hydrochloric acid. The reaction proceeded at room temperature at first and then at 30-35°. A precipitate of the nitroso compound formed gradually in the form of white crystals with m.p. 104-106°. After recrystallization from water, platelets melting at 107-108° were obtained. Yield of the recrystallized compound, 3.8 g (about 81.7% of the theoretical).

Found %: N 13.58, 13.36. $C_{10}H_{12}O_3N_2$. Calculated %: N 13.46.

Benzoylation of N-methyl-β-phenyl-β-alanine. 25 g of N-methyl-β-phenyl-β-alanine and 25 g of potassium hydroxide were dissolved in 250 ml of water, and 25 g of benzoyl chloride was added to the solution at room temperature. The reaction was conducted with mechanical stirring for 2 hours. The clear solution was then acidified with hydrochloric acid to Congo. The precipitated mixture of the bonzoyl derivative and benzoic acid was treated with boiling water. After cooling the hot solution, 5 g of benzoic acid with m.p. 110-115° precipitated from it. The undissolved residue, 29 g of benzoylmethylamino acid with m.p. 156-157°, was recrystallized from alcohol and melted at 157-158°. Yield of the benzoyl derivative was 74.5 % of the theoretical.

Found %: N 5.24, 5.30. $C_{17}H_{17}O_3N$. Calculated %: N 4.95.

Preparation of N-benzoyl-N-methyl-β-phenyl-β-alanylamide.

1) From N-methyl-β-phenyl-β-alanine. 1 g N-methyl-β-phenyl-β-alanine and 1 g of thionyl chloride were heated for 2 hours at 40-45°. The excess thionyl chloride was removed in vacuum. The obtained dark yellow oil was dissolved in dry benzene and treated with ammonia in the cold. The precipitated yellow residue was washed with benzene, water, and recrystallized from alcohol. Yield 0.79 g crystals with m.p. 172-174°, or 50.4 % of the theoretical. After recrystallization from alcohol, the melting point increased to 175-176°.

Found %: N 10.03. $C_{17}H_{18}O_2N_2$. Calculated %: N 9.93.

2) From N-methyl-β-phenyl-β-alanylamide. 0.4 g of N-methyl-β-phenyl-β-alanylamide hydrochloride was introduced into a solution of 0.2 g of sodium hydroxide in 2 ml of water. 0.27 g of benzoyl chloride was added to the solution obtained. Upon shaking, crystals with m.p. 171-172° precipitated. After recrystallization from alcohol, 0.45 g of crystals with m.p. 175-176° were obtained. The yield was about 85.5 % of the theoretical.

A mixed melting point with the N-methyl-N-benzoyl-β-phenyl-β-alanyl amide obtained in the previous experiment did not give a depression.

SUMMARY

1. The conditions for the preparation of β-phenyl-β-(N-methylamino)propionic acid were studied.

2. The hydrochloride, ethyl ester, amide, and the N-nitroso derivative of β-phenyl-β-(N-methylamino)propionic acid were prepared to characterize it.

3. The benzoylation of the phenylmethylamino acid was effected, and the synthesis of β-phenyl-β-(N-benzoyl-N-methylamino)propionamide was accomplished by two methods.

4. An attempt was made to synthesize 1-methyl-2,6-diphenyl-4-oxotetrahydropyrimidine by the dehydration of the benzoylamino acid amide by means of acetic anhydride and anhydrous oxalic acid, and it was shown that the formation of the pyrimidine derivative did not occur under these conditions.

5. The reaction of β-phenyl-β-(N-methylamino)propionamide and potassium hypobromite was studied, and it was found that 1-methyl-5-phenylglyoxalidone, which does not possess antibiotic activity, was obtained from this reaction in a 25% yield.

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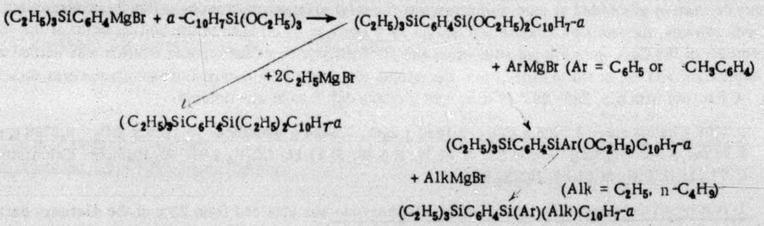
SYNTHESIS AND PROPERTIES OF SEVERAL ARYL DISILANES

P. S. Sanin

The preparation of tetracyclic monosilanes was reported by the author in a recent communication [1]. Continuing the investigation of the synthesis of high molecular silicon hydrocarbons, the synthesis of tri- and tetracyclic silanes was accomplished according to the following scheme:



$$(C_2H_5)_3SiC_6H_4MgBr + \alpha\text{-}C_{10}H_7Si(OC_2H_5)_3 \longrightarrow (C_2H_5)_3SiC_6H_4Si(OC_2H_5)_2C_{10}H_7\text{-}\alpha$$

$$\xrightarrow{+2C_2H_5MgBr} (C_2H_5)_3SiC_6H_4Si(C_2H_5)_2C_{10}H_7\text{-}\alpha$$

$$\xrightarrow{+ArMgBr\ (Ar = C_6H_5 \text{ or } CH_3C_6H_4)} (C_2H_5)_3SiC_6H_4SiAr(OC_2H_5)C_{10}H_7\text{-}\alpha$$

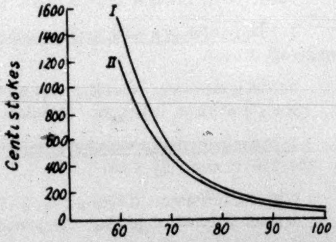
$$\xrightarrow{+AlkMgBr\ (Alk = C_2H_5,\ n\text{-}C_4H_9)} (C_2H_5)_3SiC_6H_4Si(Ar)(Alk)C_{10}H_7\text{-}\alpha$$

The tetracyclic disilanes prepared under the below-given conditions were found to be highly viscous liquids at ordinary temperatures; the change of the viscosity with temperature is given for two aromatic disilanes in the Figure.

EXPERIMENTAL

1-Triethylsilyl-4-(α-naphthyldiethoxysilyl)benzene was used as the starting material for the preparation of silicon hydrocarbons with two Si atoms, which was itself prepared from bromophenyltriethylsilane obtained under Grüttner and Krause's [3] conditions, and α-naphthyltriethoxysilane, synthesized according to Khotinsky and Serezhenkov [3]; the reaction was conducted with an excess (1.6 of theory) of triethylbromophenylsilane.

1-Triethylsilyl-4-(α-naphthyldiethoxysilyl)benzene (I). 70 g of α-naphthyltriethoxysilane, 108 g of bromophenyltriethylsilane, 12 g of magnesium, 1 g of iodine, 400 ml of ether, and 100 ml of toluene were used. An ether solution of bromophenyltriethylsilane was added in two portions to a mixture of the magnesium and the iodine in a flask equipped with a stirrer. Several minutes after the addition of the first half of the ether solution, an energetic reaction began which almost stopped within a half hour; then the second half of the ether solution of the bromophenyltriethylsilane was added, and the flask was heated on the water bath for 3 hours more at the end of the energetic reaction. The naphthyltriethoxysilane, diluted with ether (1:1) was added to the magnesium bromophenyltriethylsilane prepared in the above manner, and the reaction mass was heated for 1 hour on the water bath; the ether was then removed and replaced with toluene in which the heating was continued for 2 hours on the boiling water bath. Upon cooling the flask, the reaction mixture was treated with 20% NH_4Cl; the upper layer which separated was removed from the aqueous solution after the addition of 50 ml of ether and dried. After the removal of the ether and the toluene, the residue (130 g) was vacuum distilled at 7 mm and the following fractions were collected: 1) 65-130° (main part at 102-104°) – 28g; 2) 130-220° – 11 g; 3) 240-246° – 76 g; 4) residue – 13 g.



Variation of the kinematic viscosity with the temperature. I) 1-Triethylsilyl-4-(α-naphthyl-p-tolylethylsilyl)benzene; II) 1-triethylanil-4-(α-naphthylphenylethylsilyl)benzene.

The 1st fraction was shown to be phenyltriethylsilane upon investigation; it resulted from the decomposition of the unreacted magnesium bromophenyltriethylsilane with water.

The 2nd fraction was collected in the interval 242-245° (7 mm) upon redistillation: d_{20}^{20} 1.025.

0.1792 g substance: 0.4746 g CO_2; 0.1368 g H_2O. 0.6324 g substance: 0.1773 g SiO_2. 0.0570 g substance: 14.35 ml 0.1 N $Na_2S_2O_3$. Found %: C 72.22; H 8.54; Si 13.08; OC_2H_5 18.86. $C_{26}H_{36}Si_2O_2$. Calculated %: C 71.50; H 8.31; Si 12.86; OC_2H_5 20.64.

The increased amount of carbon and the decrease in the ethoxyl groups was caused, evidently, by the presence of impurities of the disilane $(C_2H_5)_3SiC_6H_4Si(C_2H_5)_3$, whose formation during the preparation of magnesium bromophenyltriethylsilane has been reported by Grüttner and Krause [2].

1-Triethylsilyl-4-(α-naphthyl-p-tolylethoxysilyl)benzene. The following were used: the diethoxy derivative (I), 33 g, p-bromotoluene, 106 g, magnesium, 15 g, ether 300 ml, and toluene 100 ml. An ether solution (1:1) of the diethoxy derivative was added at room temperature to the p-tolyl magnesium bromide; after the replacement of the ether with toluene, the reaction mixture was heated for 3 hours on an oil bath to the boiling point of the toluene. The contents of the flask were diluted with water and 10 % sulfuric acid; the toluene solution was washed and dried after separation, and subjected to distillation; the residue (40 g) after the removal of the toluene was vacuum distilled. A fraction with b.p. 282 - 284° (7 mm) —26 g (72%); d_{20}^{20} 1.0470 was isolated.

0.2608 g substance: 0.7438 g CO_2: 0.1880 g H_2O. 0.6424 g substance: 0.1632 g SiO_2. 0.0788 g substance: 8.57 ml 0.1 N $Na_2S_2O_3$. Found %: C 77.78; H 8.06; Si 11.85; OC_2H_5 8.80. $C_{31}H_{38}Si_2O$. Calculated %: C 77.11; H 7.95; Si 11.63; OC_2H_5 9.32.

1-Triethylsilyl-4-(α-naphthylphenylethoxysilyl)benzene was obtained from 33 g of the diethoxy derivative (I) under the above reported conditions in an 80% yield in the form of a viscous yellow liquid with b.p. 274-276° (7 mm) and d_{20}^{20} 1.055.

0.2076 g substance: 0.5914 g CO_2; 0.1444 g H_2O. 0.5730 g substance: 0.1453 g SiO_2. 0.1048 g substance: 12.84 ml 0.1 N $Na_2S_2O_3$. Found %: C 77.69; H 7.78; Si 11.83; OC_2H_5 8.90, $C_{30}H_{36}Si_2O$. Calculated %: C 76.86; H 7.75; Si 11.98; OC_2H_5 9.61.

The following silicon hydrocarbons were synthesized by substituting alkyl groups for ethoxy groups in the ethoxy derivatives obtained under conditions reported for the preparation of monosilanes [1].

1-Triethylsilyl-4-(α-naphthyldiethylsilyl)benzene with a yield of 76% of the theoretical: b.p. 249-252° (7 mm); d_{20}^{20} 0.9943.

0.1958 g substance: 0.5562 g CO_2; 0.1614 g H_2O . 0.6268 g substance: 0.1890 g SiO_2. Found %: C 77.47; H 9.22; Si 14.07. $C_{26}H_{3}Si_2$. Calculated %: C 77.15; H 8.97; Si 13.88.

1-Triethylsilyl-4-(α-naphthylphenylethylsilyl)benzene with a yield of 90% of the theoretical; b.p. 276-278° (7 mm); d_{20}^{20} 1.0406.

0.2206 g substance: 0.6466 g CO_2; 0.1612 g H_2O 0.6250 g substance: 0.1607 g SiO_2. Found %: C 79.84; H 8.17; Si 12.00. $C_{30}H_{36}Si_2$. Calculated %: C 79.57; H 8.02; Si 12.41.

1-Trimethylsilyl-4-(α-naphthyl-p-tolylethylsilyl)benzene was obtained with a yield of 85% of the theoretical: b.p. 284-286° (7 mm); d_{20}^{20} 1.035.

0.2246 g substance: 0.6568 g CO_2; 0.1700 g H_2O. 0.6022 g substance: 0.1379 g SiO_2. Found %: C 79.70; H 8.46; Si 10.67. $C_{31}H_{38}Si_2$. Calculated %: C 79.76; H 8.21; Si 12.03.

1-Triethylsilyl-4-(α-naphthyl-p-tolyl-n-butylsilyl)benzene was obtained with a yield of 60% of the theoretical; b.p. 293-295° (7 mm); d_{20}^{20} 1.024.

0.2234 g substance: 0.6554 g CO_2; 0.1700 g H_2O. 0.7168 g substance: 0.1587 g SiO_2. Found %: C 80.01; H 8.51; Si 10.33. $C_{33}H_{42}Si_2$. Calculated %: C 80.08; H 8.56; Si 11.36.

The last three disilanes are thick, poorly mobile, yellow colored liquids.

The determination of the carbon and hydrogen for all of the compounds synthesized was effected by the combustion of the sample of the substance in a tube with copper oxide. The silicon was determined by means of oxidation with concentrated H_2SO_4 in the presence of K_2SO_4 and $CuSO_4$, and the ethoxyl groups according to Kreshkov and Nessonova [4].

SUMMARY

The following were newly synthesized: 1-triethylsilyl-4-(α-naphthyldiethoxysilyl)benzene, 1-triethylsilyl-4-(α-naphthyl-p-tolylethoxysilyl)benzene, 1-triethylsilyl-4-(α-naphthylphenylethoxysilyl)benzene, and the silicon hydrocarbons: 1-triethylsilyl-4-(α-naphthyldiethylsilyl)benzene, 1-triethylsilyl-4-(α-naphthylphenylethylsilyl)benzene, 1-triethylsilyl-4-(α-naphthyl-p-tolylethylsilyl)benzene, 1-triethylsilyl-4-(α-naphthyl-p-tolyl-n-butylsilyl)benzene.

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* See Consultants Bureau Translation, p. 1167.

A NEW METHOD FOR THE SYNTHESIS OF ORTHO DERIVATIVES OF BENZOTRIFLUORIDE

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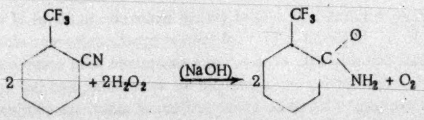
The trifluoromethyl group is an electropositive meta-directing group; for this reason, the meta derivatives of benzotrifluoride have been the most accessible and investigated. A method for the synthesis of para derivatives has also been reported [1]. The ortho-substituted benzotrifluorides have remained the least accessible. Up to now, they were prepared by means of o-aminobenzotrifluoride [1].

In 1951, a method for the preparation of o-bromobenzotrifluoride was reported which consisted of the metalization of benzotrifluoride with butyl lithium followed by the substitution of the lithium by bromide [2]. The yield of o-bromobenzotrifluoride was 28% of the theoretical. o-Trifluoromethylbenzoic acid was prepared from it. The low yield of o-bromobenzotrifluoride, and the complexity of its preparation, lowers the value of the above method.

The authors decided to try and find a simpler and more convenient method for the synthesis of o- derivatives of benzotrifluoride. The possibility for the preparation of o-trifluoromethylbenzonitrile from the corresponding trichloromethyl derivative [3] was investigated for this purpose. The fluorination of o-trichloromethylbenzonitrile with antimony trifluoride was found to proceed smoothly with a yield of 78%. This made possible its use as a starting material for the synthesis of ortho derivatives of benzotrifluoride.

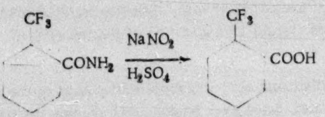
o-Trifluoromethylbenzonitrile is reported in the literature. It was prepared from the corresponding, difficultly accessible, amine in low yield. It, evidently, was not isolated in the pure form. The reported m.p. +7.5° [4] is incorrect; an m.p. +18° was found. Several derivatives were obtained from o-trifluoromethylbenzonitrile. These substances were known previously. However, the methods used by the authors for their synthesis were simpler and gave considerably better yields. Thus o-trifluoromethylbenzamide was prepared in an 87% of the theoretical yield from o-trifluoromethylbenzonitrile by the action of 30% hydrogen peroxide, in the presence of alkali, on an alcoholic solution of the nitrile, according to Radziszewski [5].



The amide of o-trifluoromethylbenzoic acid was previously prepared by heating its methyl ester for 36 hours at 110° in a sealed tube with concentrated ammonia solution, [6].

o-Trifluoromethylaniline, which previously served as starting substance for the synthesis of ortho derivatives of benzotrifluoride, was obtained in a yield of 72% of the theoretical from o-trifluoromethylbenzamide by the Hoffman reaction.

o-Trifluoromethylbenzoic acid was previously synthesized (in addition to the above reported method with the aid of lithium organo-compound) by boiling the nitrile with 10% sodium hydroxide for 80 hours [6]. A considerable amount of phthalic acid was also obtained. o-Trifluoromethylbenzoic acid was obtained from its amide by Bouveault's method [7]:



The hydrazide, unreported in the literature, was obtained from ethyl o-trifluoromethylbenzoate which was synthesized by the authors, by boiling it for many hours with hydrazine hydrate.

The above difficulty in converting ethyl o-trifluoromethylbenzoate into the hydrazide, as well as the difficulty mentioned in the literature in preparing the methyl ester (two day boiling of the acid with hydrogen chloride in methyl alcohol [6]) and the amide [6], indicates, evidently, that the CF_3 group causes steric hindrance.

EXPERIMENTAL

o-Trichloromethylbenzonitrile [3]. 20 g of o-tolylnitrile prepared from o-toluidine [8] was placed into a 100 ml round bottom flask equipped with a two necked adapter. A bubbler was introduced through one of the necks and the other one was connected to a condenser protected by calcium chloride tube. The flask was heated on an oil bath to 150°, illuminated by a mercury lamp, and chlorine was passed in through the bubbler until an increase in weight of 17 g. The oil bath temperature was gradually increased to 185° during the process of chlorination. The reaction mass was vacuum distilled. Two fractions were collected: 1) up to a constant boiling point at 8 mm, 11.2 g, 2) b.p. 151-152° at 8 mm, 22.16 g. Both fractions crystallized at the same time. M.p. of Fraction 1, 85-87°. Melting point of Fraction 2, 94-95°, corresponding to that reported in the literature [3] for o-trichloromethylbenzonitrile. 10.1 g of the product with m.p. 94-95° was isolated from Fraction 1 after recrystallization from alcohol. The total yield was 35.26 g or 86% of the theoretical.

o-Trifluoromethylbenzonitrile. 20 g of o-trichloromethylbenzonitrile was mixed with 20 g of antimony trifluoride in a 100 ml Wurtz flask. The mixture was heated until a homogenous liquid formed and distilled. The distillate was dissolved in a mixture of ether and 6 N hydrochloric acid, the ether layer was washed several times with 6 N hydrochloric acid until complete removal of the $SbCl_3$, then 1-2 times with water, and dried over anhydrous Na_2SO_4. The ether was removed and the residue distilled. B.p. 204-206°. Yield 11.9 g. The substance readily crystallized in an ice bath and had an m.p. 18°. Found %: N 8.28, 8.22. $C_8H_4NF_3$. Calculated %: N 8.18.

o-Trifluoromethylbenzamide. 13 g of o-trifluoromethylbenzonitrile, 50 ml of 95% ethyl alcohol, 33 ml of 30% hydrogen peroxide, and 5 ml of 6 N sodium hydroxide were placed into a 250 ml round bottom flask. The mixture started to evolve oxygen at once. The reaction was accompanied by a strong evolution of heat. The temperature was kept at 40-50° by external cooling. The exothermic reaction moderated noticeably after 1 hour, and the mixture was left to stand overnight. The mixture was then heated for 3 hours to 50° on the water bath and then cooled to 0°. The precipitated crystals were filtered, washed with water, and dried (11 g). M.p. 160-161°, which coincides with that reported in the literature [6]. The filtrate was diluted with an equal volume of water and again cooled to 0°; 1.5 g more of the amide with m.p. 160° formed. Total yield, 12.5 g.

o-Trifluoromethylaniline. A solution of 10 g of sodium hydroxide in 80 ml of water was cooled to 0°, and 2.5 ml of bromine was added to it. The cold solution of sodium hypobromite was added to 8 g well pulverized o-trifluoromethylbenzamide in a 150 ml flask. The mixture was mixed until complete solution of the amide and placed on a boiling water bath. The heating was continued for 45 minutes, and the flask was cooled to room temperature. The amine was extracted with three 15 ml portions of ether, the combined ether extracts were dried with anhydrous Na_2SO_4, the ether removed, and the o-trifluoromethylaniline vacuum distilled. M.p. 65-67° at 15 mm. Yield 4.9 g. The acetyl derivative, obtained from the amine and acetic anhydride in pyridine, had an m.p. 94-95° (reported in the literature, m.p. 94.5° [6]).

o-Trifluoromethylbenzoic acid. 14.4 g of o-trifluoromethylbenzamide was suspended in 72 ml of water in a 500 ml three necked flask equipped with stirrer, thermometer and dropping funnel whose tip was drawn into a capillary going to the bottom of the flask. 36 ml of concentrated sulfuric acid was added to the mixture with stirring. The mixture was heated to 98°. The amide dissolved completely. 12 g of sodium nitrite in 180 ml of water was added to the solution with efficient stirring from the dropping funnel. The temperature of the reaction mixture was kept at 98-100°; it was neceassary to heat the flask from time to time. After the addition of $NaNO_2$ solution, the flask was cooled with cold water, and the acid extracted from the solution with three 25 ml portions of ether. The combined ether extracts were shaken with a solution of sodium hydroxide. The aqueous layer was separated and acidified with concentrated hydrochloric acid. The precipitated o-trifluoromethylbenzoic acid was filtered, washed with water, and dried. Yield 13.2 g or 91% of the theoretical. M.p. 107-108° (an m.p. 108.5° [6] is given in the literature).

The ethyl ester of o-trifluoromethylbenzoic acid was prepared by heating the acid chloride with absolute ethyl alcohol. The product was washed with water, dried over Na_2SO_4, and vacuum distilled. B.p. 90-91° at 10 mm.

o-Trifluoromethylbenzoic hydrazide was prepared by boiling the ethyl ester of this acid with hydrazine for 3 hours. The product was recrystallized from aqueous alcohol. M.p. 134°.

Found %: N 13.55, 13.63. $C_8H_7ON_2F_3$. Calculated %: N 13.72.

SUMMARY

A new way of synthesizing ortho derivatives of benzotrifluoride has been found, making it possible to prepare o-trifluoromethylbenzonitrile, o-trifluoromethylbenzoic acid, and o-trifluoromethylaniline, while it may also be employed in the preapration of other compounds not described hitherto.

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SYNTHESIS OF CYCLOHEPTANE DERIVATIVES WITH THE AID OF ACETOACETIC ESTER

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In one of the previous communications [1], it was shown that, if the reaction for the formation of cycloheptane-1,1-dicarboxylic ester with the aid of malonic ester was conducted in two stages, the yield of the substance was considerably increased. Cycloheptane-1,1-dicarboxylic acid, previously unreported in the literature, was obtained by saponifying it. It appeared to be of interest to also try and prepare seven membered rings with the aid of acetoacetic ester since, as far as it is known, the given reaction has not been studied by anyone up to now.

For this purpose, ζ-iodohexylacetoacetic ester (I), unreported up to now, was initally synthesized in the present investigation by the action of sodio acetoacetic ester on hexamethylene iodide.

$$CH_2(CH_2)_4CH_2CH(COCH_3)COOC_2H_5.$$

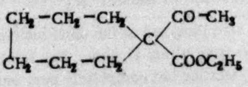
(I)

The yield of the above compound, as it had been previously shown with other examples [2], varied with the amount of the dihalo derivative used in each separate case. Thus for example, if 1 g atom of metallic sodium (in the form of the alcoholate), 4 moles of acetoacetic ester, and 1 mole of hexamethylene iodide were used for the reaction, ζ-iodohexylacetoacetic ester was obtained in a yield of 33.1% of the theoretical. If the amount of hexamethylene iodide used was 2 times greater than required by calculations, then the yield of the haloalkylacetoacetic ester was increased to 65.4% of the theoretical.

With a 3 fold quantity of the dihalo derivative, ζ-iodohexylacetoacetic ester was formed with a yield equal to 74.7% of the theoretical.

The yields, calculated on the basis of previously given theoretical considerations [2], were equal to 36.6, 60.4, and 72.4%, respectively, of theory. Therefore, there is a satisfactory agreement of the yields obtained experimentally in the given case with those calculated on the basis of the law of mass action.

The second stage of the reaction, i.e., the cyclization of ζ-iodohexylacetoacetic ester (I), was conducted in dilute (0.22 molar) alcoholic solution. It was found that the normal reaction product, 1-acetylcycloheptane-1-carboxylic ester (II), formed in a yield of about 32% of theory was subjected to alcoholysis to a considerable extent with the formation of acetoacetic ester and the ethyl ester of cycloheptanecarboxylic acid.



(II)

For this reason, a mixture was formed in the end which consisted of the ethyl ester of cycloheptanecarboxylic acid (yield 25.5% of the theoretical) and 1-acetylcycloheptane-1-carboxylic ester (yield about 6%). The latter compound was characterized by means of its semicarbazone. In addition, a large amount of high molecular condensation products was obtained.

The alcoholysis of dialkylated esters of β-keto acids under the catalytic effect of alcoholate has been observed many times in the past [3]. The cleavage of 1-acetylcyclopentane-1-carboxylic ester formed by the action of sodio acetoacetic ester on tetramethylene bromide [4], was also found to occur with the formation of the ethyl ester of cyclopentanecarboxylic acid by the effect of sodium alcoholate.

EXPERIMENTAL

The hexamethylene iodide necessary for the investigation was prepared by means of a previously reported method [1], and had a b.p. 135-138° at 6 mm.

ζ-Iodohexylacetoacetic ester. 4.6 g (0.2 g atoms) of metallic sodium was dissolved in 75 ml of absolute alcohol, and then 104 g (0.8 mole) of freshly distilled acetoacetic ester (b.p. 70° at 13 mm) followed by 203 g (0.6 mole) of hexamethylene iodide was added to the alcoholate solution. After heating the reaction mixture to boiling on a bath for 4 hours and cooling, the reaction product was poured into water and extracted with ether. The ether extracts were washed with a weak solution of hyposulfite, dried with fused calcium chloride, the ether was then removed, and the residue fractionated in vacuum. 125 g of hexamethylene iodide was recovered (a fraction with b.p. 132-139° at 6 mm), and 58 g of a fraction with b.p. 155-186° (mainly at 168-177°) at 6 mm was obtained. Upon redistillation of this fraction, an average of 50.6 g (74.4% of the theoretical) of a colorless oily liquid which rapidly yellowed, was isolated at 152-156° (1.5 mm); d_4^{20} 1.3607; n_D^{20} 1.4947; MR_D 72.82. $C_{12}H_{21}O_3I$. Calculated: for the enolic form 73.32; for the ketonic 72.18; average 72.75 .

0.3481 g substance: 0.5452 g CO_2; 0.1965 g H_2O. 0.3281 g substance: 0.2274 g AgI (according to Carius). Found %: C 42.71; H 6.28; I 37.46. $C_{12}H_{21}O_3I$. Calculated %: C 42.35; H 6.18; I 37.35.

In a second experiment, 44.5 g (65.4%) of ζ-iodohexylacetoacetic ester was obtained from 4.6 g (0.2 g-atom) of sodium, dissolved in 75 ml of absolute alcohol, 104 g (0.8 mole) of acetoacetic ester, and 135 g (0.4 mole of hexamethylene iodide.

In a third experiment, 22.5 g or 33.1% of the theoretical of ζ-iodohexylacetoacetic ester was obtained with the use of the theoretical amount (68 g or 0.2 mole) of hexamethylene iodide.

Cyclization of ζ-iodohexylacetoacetic ester. 3.45 g (0.15 g atom) of metallic sodium was dissolved in 650 ml of absolute alcohol, 51 g (0.15 mole of ζ-iodohexylacetoacetic ester was added, and the mixture was heated for 3 hours to boiling. The main part of the alcohol was distilled off (a distinct odor of acetoacetic ester was detected in the distillate), the residue was poured into water, the reaction products extracted with ether, the ether extracts washed with a dilute hyposulfate solution, dried with fused $CaCl_2$, the ether removed, and the residue fractionated in vacuum. 6.5 g of a substance boiling at 72-76° at 3 mm and 2 g of fraction with b.p. 102-104° at 2 mm were obtained. A large amount of a thick residue remained in the flask. The fraction with b.p. 72-75° upon redistillation, boiled mainly at 74° at 3 mm and was the ethyl ester of cycloheptane carboxylic acid. (Yield 25.5 % of the theoretical).

d_4^{20} 0.9515; n_D^{20} 1.4482; MR_D 47.84; Calc. 47.83.

0.2234 g substance: 0.5758 g CO_2; 0.2165 g H_2O. Found %: C 70.29; H 10.76. $C_{10}H_{18}O_2$. Calculated %: C 70.59; H 10.59.

6 g of the cycloheptanecarboxylic ester was saponified with an aqueous alcoholic potassium hydroxide solution, the alcohol removed, the residue acidified with sulfuric acid, and the precipitated liquid acid extracted with ether. The ether extracts, dried with fused $CaCl_2$, left an acid, after the removal of the solvent, which was distilled at ordinary pressure (709 mm) where it boiled at 248-251° [5]. Yield was 3.9 g (78% of the theoretical).

The amide of cycloheptanecarboxylic acid obtained in the usual manner [1] (by means of the acid chloride), melted at 195-196° [5] after 2 recrystallizations from dilute alcohol. The fraction with b.p. 102-104°, according to constants and results of elementary analysis, was the not completely pure ester of 1-acetylcycloheptane-1-carboxylic acid. For this reason, it was treated in the cold with a solution of semicarbazide. The separation of crystals started on the following day. Several days later, the crystals were filtered and twice recrystallized from alcohol, after which they melted at 193-194°.

0.1122 g substance: 0.2392 g CO_2; 0.0900 g H_2O. 0.0865 g substance: 9.55 ml 0.1 NH_2SO_4 (according to Kjeldahl). Found %: C 58.05; H 8.91; N 15.46. $C_{13}H_{23}O_3N_3$. Calculated %: C 58.00; H 8.55; N 15.61.

SUMMARY

1. ζ-Iodohexylacetoacetic ester was obtained by the action of sodio acetoacetic ester on hexamethylene iodide. By using 1 mole of hexamethylene iodide for 1 mole of sodium alcoholate and 4 moles of acetoacetic ester, the yield of ζ-iodohexylacetoacetic ester was equal to 33.1% of the theoretical. By using twice the

theoretical amount of hexamethylene iodide, the yield of the reaction product was 65.4% and with a 3-fold amount, 74.4% of the theoretical. The yields obtained agree satisfactorily with those calculated on the basis of the mass action law.

2. Upon cyclization of ζ-iodohexylacetylacetic ester with the aid of sodium alcoholate in an 0.22 molar alcoholic solution, 1-acetylcycloheptane-1-carboxylic ester was formed in a yield of about 33% of the theoretical. During the process of the reaction it was subjected to alcoholysis to a considerable degree and was converted into the ethyl ester of cycloheptanecarboxylic acid.

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* See Consultants Bureau Translation, p. 871.

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INVESTIGATION OF THE PROCESS OF ISOMERIZATION AND DIMERIZATION OF DIMETHYLVINYLCARBINOL IN RELATION TO THE pH OF THE REAGENT

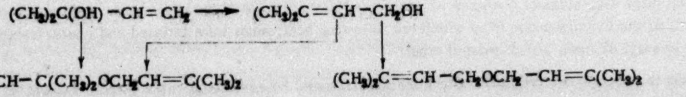
II. ACTION OF A SATURATED SOLUTION OF CUPROUS CHLORIDE IN HYDROCHLORIC ACID ON DIMETHYLVINYLCARBINOL

A. I. Lebedeva and L. F. Almashi

From previously published communications it is known [1,2,3] that sulfuric acid causes dehydration, allylic rearrangement, and condensation of dimethylvinylcarbinol, as a result of which are formed isoprene, primary γ,γ-dimethlallylic alcohol, linalool, geraniol, and terpin hydrate. In the previous communication, A.I. Lebedeva and L.L. Shchukovskaya [4] reported the start of an investigation of the various transformations of dimethylvinylcarbinol in relation to the pH of the acting reagent. In the present investigation, it was decided to continue this investigation at higher hydrogen ion concentrations and to study the action of a saturated solution of cuprous chloride in hydrochloric acid of various concentrations: 1 N, 5 N, and 10 N on dimethylvinylcarbinol. It was found that under the conditions investigated, the removal of water occurs not only from one molecule of the alcohol with the formation of isoprene, but also from two molecules, leading to formation of ethers of dimethylvinylcarbinol and γ,γ-dimethylallylic alcohol, isomeric with it, γ,γ-dimethylallylic ether of 2-methyl-2-butene-4-ol (I) and γ,γ-dimethylallylic ether of 2-methyl-3-butene-2-ol (II).

On the basis of the experiments conducted, it cannot be stated with complete certainty that the formation of the ethers occurs by means of a chloride stage with the subsequent cleavage of HCl from a molecule of the chloride and the alcohol, but a possibility for this occurrence exists. It is known from I.N. Nazarov and I. N. Azerbaeva's [5] investigation that the replacement of a hydroxyl by a chlorine occurs very readily even at 0°. by the action of gaseous hydrogen chloride on dimethylvinylcarbinol resulting in a mixture of primary and tertiary chlorides.

The reaction forming the unsaturated ethers from dimethylvinylcarbinol can be represented schematically in the following manner:


$(CH_3)_2C(OH)-CH=CH_2 \longrightarrow (CH_3)_2C=CH-CH_2OH$
$H_2C=CH-C(CH_3)_2OCH_2CH=C(CH_3)_2$
$(CH_3)_2C=CH-CH_2OCH_2-CH=C(CH_3)_2$

(II) (I)

From the results obtained (Table 1), it can be seen that decreasing the pH of the solution of cuprous chloride leads to the increase in the yield of the primary-primary ether, and conversely, the yield of the primary-tertiary ether is increased with the increase in pH. These findings correspond to the results of I.N. Nazarov and co-workers [6] on the obtaining of methyl ethers from dimethylvinylcarbinol; it was shown that the ratio of the isomeric ethers depends on the concentration of sulfuric acid.

A complex mixture was obtained as a result of a several-day action of the above solution of cuprous chloride in hydrochloric acid on dimethylvinylcarbinol, from several individual compounds (1-5) were isolated upon many redistillations through a column, having the following boiling points: 1) 34-36°, 2) 97-98°, 3) 49° (10 mm), 4) 40° (3 mm), 5) 55° (3 mm) (Table 1). The higher boiling fraction has not been investigated further as yet. Compound 1 corresponds to isoprene according to its constants, 2, starting dimethylvinylcarbinol, 3 primary γ,γ-dimethylallylic alcohol.

The structure of compound 4 with b.p. 40° (3 mm) was determined by ozonolysis, study of Raman spectra, and catalytic hydrogenation in the presence of platinum.

The investigation of the ozonolysis products did not give any definite results even if it is assumed that the ozonolysis occurs according to the scheme given by Ya. M. Slobodin [7] for substances having an allylic group in their composition; for this reason a Raman spectrum was taken for the substance. A photograph of the Raman spectrum is given in the Figure. (See Plate, page 1115).

It is known, [8, 9], that the frequency 1675 cm^{-1} is characteristic for secondary-tertiary double bonds, frequency 1640 cm^{-1} for primary-secondary double bonds, and 1413 cm^{-1} for an end methylene group.

The catalytic hydrogenation of compound 4 in the presence of platinum black at room temperature and atmospheric pressure was of great interest. Under these conditions, the cleavage of this compound with hydrogen occurred with the formation of isopentane, amylene hydrate, and primary isoamyl alcohol. 3 molecules of hydrogen were consumed for each molecule of the compound consumed even though it only had 2 double bonds (which was determined by the bromine number).

It was found that after the addition of one molecule of hydrogen, the bromine number decreases (which is apparent from the number of milliliters of bromide-bromate consumed for the titration), and a hydroxyl appears.

The hydrogenation under the given conditions does not occur slectively: simultaneously with the addition of hydrogen at the double bond, a cleavage of the ether bond occurs with the formation of compounds containing a hydroxyl (Table 2).

The absence of a positive reaction for a hydroxyl and carbonyl group, with the presence of one atom of oxygen in the molecule, the investigation of the Raman spectrum, and the results of the catalytic hydrogenation meant that compound 4 must have been the γ,γ-dimethylallylic ether of 2-methyl-3-butene-2-ol (II).

The cleavage of the ether bond under such mild conditions is only reported in one paper [10], in which the authors were able to cleave an ether bond with phenyl radicals during hydrogenation over platinum oxide in glacial acetic acid.

Compound 5 had a very sharp odor, which caused a headache. The analyses showed that the compound had a general formula $C_{10}H_{18}O$. The hydroxyl determination according to Terentyev-Shcherbakova, gave negative results. The substance was hydrogenated catalytically in the presence of platinum black in absolute ether. More than three molecules of hydrogen were absorbed per molecule of the compound. A mixture was obtained as a result of the hydrogenation from which the following ocmpounds were isolated and characterized: isopentane, primary isoamyl alcohol, and diisoamyl ether.

On the basis of all the given determinations, it could be considered that compound 5 was γ,γ-dimethylallyl 2-methyl-2-butene-4-yl ether.

Therefore, unsaturated ethers were obtained from dimethylvinylcarbinol and it was shown that the ether bond in the compounds of the above structure was readily cleaved with hydrogen in the presence of platinum black at atmospheric pressure and room temperature.

EXPERIMENTAL

Technical dimethylvinylcarbinol, b.p. 96-97° containing about 85% of the pure substance was used for all experiments. The percent content of dimethylvinylcarbinol was determined by catalytic hydrogenation in the presence of platinum black and bromination with an aqueous solution of bromide-bromate. The total concentration of hydrochloric acid was the same for each experiment, only the concentration of the solution used was varied. The solution of hydrochloric acid used for the experiment was saturated with cuprous chloride by prolonged shaking. The pH of the solution was determined prior to and after saturation with glass electrodes. The experiments were conducted in a three-necked flask equipped with a stirrer, dropping funnel, and a long reflux condenser. The solution of cuprous chloride in hydrochloric acid was added slowly with stirring to the dimethylvinylcarbinol in the flask. 50 g of dimethylvinylcarbinol were used for every experiment. The mixture was stirred efficiently for 60 hours at room temperature, 3 hours at 30-40°, and 3 hours at 70-80°. The upper and lower layers were then separated, the upper layer was washed with aqueous sodium carbonate solution, and dried with fused potassium carbonate. After drying, the upper layer was separated into several fractions by simple distillation which were then each subjected to fractional distillation on a column fitted with a complete condensation head. The lower layer was extracted with ether for 48 hours in a percolator. Only a small amount of dimethylvinylcarbinol was isolated from the lower layer after the removal of the ether; it did not contain any other products. The results of the experiments conducted are given in Table 1.

TABLE 1

Exp. No.	Amt. of saturated cuprous chloride in hydrochloric acid used for the reaction (in g)	Concentration hydrochloric acid used for the reaction	pH of the hydrochloric acid	pH of the saturated cuprous chloride solution in hydrochloric acid	Yield of substance with b.p. 34-36° (in g)	Yield of substance with b.p. 97-98° (in g)	Yield of substance with b.p. 40° (10 mm) (in g)	Yield of substance with b.p. 40° (3mm) (in g)	Yield of substance with b.p. 55° (3mm) (in g)	Yield of substance with b.p. 74-76° (10 mm) (in g)	Residue in distillation flask (in g)
1	50	1 N	−0.05	−0.15	2.0	10.2	4.0	9.0	1.5	1.0	2.5
2	10	5 N	−0.43	−0.55	4.0	10.0	6.5	5.0	1.5	–	8.0*
3	5	10 N	−0.73	−1.1	2.0	15.0	2.0	7.5	3.1	5.5	12.0

* In this experiment, the fraction with b.p. 74-76° (3 mm) was not isolated.

Analysis of Fraction 1 with b.p. 34-36°

n_D^{17} 1.4150; d_4^{17} 0.6805; MR_D 25.05. $C_5H_8F_2$. Calculated 24.36.

Analysis of Fraction 2 with b.p. 97-98°

n_D^{24} 1.4110; d_4^{24} 0.8097; MR_D 26.42. $C_5H_{10}O'F$. Calculated 26.35.

Analysis of Fraction 3 with b.p. 40° (10 mm)

n_D^{20} 1.4410; d_4^{20} 0.8680; MR_D 26.21. $C_5H_8O'F$. Calculated 26.35.

0.2107 g substance: 16.4 g benzene Δt 0.80°. 0.1050 g substance: 28.5 ml CH_4 (20°, 761.2 mm). Found: M 81.91; number of active H 0.95. C_5H_8O. Calculated: M 86.16; number of active H 1.00.

Analysis of Fraction 4 with b.p. 40° (3mm)

The compound had a pleasant odor; its optimum yield was about 30 % based on the dimethylvinylcarbinol reacted.

n_D^{16} 1.4423; n_α^{16} 1.4399; n_β^{16} 1.4503; d_4^{16} 0.8332; MR_D 48.92; MR_α 48.74; MR_β 49.69.

$C_{10}H_{18}OF_2$. Calculated: MR_D 49.26; MR_α 48.80; MR_β 49.75.

0.1028 g substance: 0.2923 g CO_2; 0.1067 g H_2O. 0.1270 g substance: 0.3613 g CO_2; 0.1308 g H_2O. 0.2281 g substance: 15.3 g benzene: Δt 0.50°. 0.2100 g substance: 24.5 ml bromide-bromate (T 0.01732 g/ml). Found %: C 77.61, 77.64; H 11.61, 11.52; M 151.6. Bromine number 312. $C_{10}H_{18}O$. Calculated: C 77.87; H 11.76; M 154.22. Bromine number 319.66.

2 g of the substance was ozonized in chloroform solution (30 ml) at -70°. 1.5 g of ozone added; 2.7 g of the ozonide remained after the filtration of the chloroform. The ozonide was decomposed with water, and the solution obtained was diluted to 500 ml with water.

Formic acid was determined in 50 ml of the solution by Finke's [11] method. 1.2790 g of Hg_2Cl_2 was obtained. Formaldehyde was determined in another 50 ml with dimedon. The weight of the dimedon derivative obtained was 0.0588 g, m.p. 188-189°. The total amount was 1.4 g based on the formic acid. About three molecules of formic acid were formed for a molecule of the compound. Potassium carbonate was added to a distinctly alkaline reaction to the solution remaining after the removal of the formaldehyde with dimedon and the neutral product then steam distilled into a sulfuric acid solution of 2,4-dinitrophenylhydrazine. The melting point of the 2,4-dinitrophenylhydrazone obtained was 125-126°. A mixed melting point with authentic acetone 2,4-dinitrophenylhydrazone gave no depression. Other neutral products were not detected. The rest of the solution was then worked up in the usual manner to isolate, first, the volatile acids, and then the nonvolatile acids. None of these was found in the ozonolysis products.

The Raman spectrum of the compound was taken at an exposure of 1.5 hours and slit of 0.1 mm. A blue (λ =22938 cm^{-1}) line was used as the excitation line. The following frequencies (cm^{-1} were obtained: (the intensities were evaluated visually and their relative values are given in the parentheses): 300 (2); 454 (1); 437 (5); 822 (2); 883 (3); 926 (4); 1044 (2); 1116 (0.5); 1154 (0.5); 1239 (1); 1247 (0.25); 1294 (3); 1326 (2); 1379 (6); 1413 (1.5); 1446 (6); 1640 (4); 1675 (6); 2793 (7); 2866 (1); 2923 (4); 2993 (1); 3046 (0.5); 3138 (0.25).

Catalytic hydrogenation of compound 4. 7.57 g of the substance: 0.8 g of Pt, 30 ml of absolute ether 3526 ml of H_2 (18°, 763 mm) was absorbed, 100.8 % of the theoretical (if 3 molecules of hydrogen are assumed).

The solution, after the filtration of the platinum, was distilled. The fraction boiling within the limits 30-36° was shaken with concentrated hydrochloric acid in a separatory funnel; the upper layer was separated from the hydrochloric acid ether solution, washed with sodium carbonate solution, dried with $CaCl_2$, and was distilled; a fraction boiling at 31-32° (1.0 g) was collected

n_D^{17} 1.3540; d_4^{17} 0.6193; MR_D 25.31. Calculated 25.29.

0.2570 g substance: 16.8 g benzene: Δt 1.65°. Found: M 67.23. C_5H_{12}. Calculated: M 72.1.

The data obtained corresponded to isopentane.

Two individual compounds were isolated from the substance remaining after the distillation of the ether, by distilling it through a column with a complete condensation head; the first with b.p. 101-102° (1.6 g)

n_D^{14} 1.4055; d_4^{14} 0.8062; MR_D 26.81; Calculated 26.82.

0.0917 g substance: 24.8 ml CH_4 (20°, 759 mm). Found: number of active H 0.97. $C_5H_{11}OH$. Calculated: number of active H 1.00.

The qualitative Denige reaction (formation of a yellow precipitate) characteristic for tertiary alcohols was positive.

The data obtained corresponded to tertiary amyl alcohol, amylene hydrate.

The second compound boiled at 131-132° (0.5 g).

n_D^{17} 1.4080; d_4^{17} 0.8132; MR_D 26.75; Calculated 26.82.

0.0901 g substance: 25.0 ml CH_4 (17°, 761 mm). Found: number of active H 1.00. $C_5H_{11}OH$. Calculated: number of active H 1.00.

The theoretical amount of an α-naphthylurethane with m.p. 67-68° was obtained from 0.3 g of the compound, which corresponded to the melting point of primary isoamyl alcohol α-naphthylurethane.

3 g of compound 4 was dissolved in 60 ml of absolute ether and hydrogenated catalytically in the presence of 0.3 g of Pt black. 2 ml samples were removed from the solution and the amount of bromide-bromate necessary to titrate it and the amount of methane spearated during the determination of the hydroxyl measured. The analysis was conducted with the starting substance after the addition of one molecule of hydrogen, after the addition ot two molecules, and finally, after the addition of three molecules.

The results of the analyses are given in Table 2.

TABLE 2

Name of Sample	Amount of bromide-bromate (in ml)	Amount of CH_4 (in ml)
Starting substance	12.5	0
After addition of one molecule of hydrogen	9.1	6.9
After addition of two molecules of hydrogen	2.9	13.5
After addition of three molecules of hydrogen	0	15.5

Analysis of Fraction 5 with b.p. 55° (3 mm)

The compound had a very sharp odor, its optimum yield was about 16% based on the amount of dimethylvinylcabinol reacted.

n_D^{15} 1.4500; n_{α}^{16} 1.4437; d_4^{16} 0.8380; MR_D 49.45; MR_{α} 48.85. $C_{10}H_{18}O\overline{|}_{2}$. Calculated MR_D 49.26; MR_{α} 48.80.

0.1220 g substance: 0.3474 g CO_2; 0.1263 g H_2O. 0.1230 g substance: 0.3501 g CO_2; 0.1271 g H_2O. 0.2611 g substance: 14.17 g benzene: Δt 0.630°. Found %: C 77.70, 77.68; H 11.59, 11.57; M 151.5. $C_{10}H_{18}O$. Calculated: C 77.87; H 11.76; M 154.2.

A negative reaction was obtained upon the determination of the hydroxyl according to Terentyev-Shcherbakova.

Catalytic hydrogenation of compound 5. 3.35 g of the substance, 0.3 g Pt, 30 ml of absolute ether. 1900 ml of H_2 was consumed (18°, 759 mm), 122% of the theoretical (based upon 3 molecules of hydrogen).

The solution was processed in the same manner as for the hydrogenation of compound 4. The first fraction boiling at 31-32° corresponded to isopentane. The second boiling at 131-132° (0.5 g) gave an α-naphthylurethane with m.p. 67-68° corresponding to primary isoamyl alcohol The third fraction (0.4 g) boiled at 173-175°, n_D^{17} 1.4100.

0.2000 g substance: 15.2 g benzene: Δt 0.43°. Found: M 156.3. $C_{10}H_{22}O$. Calculated M 158.3.

The data corresponded to diisoamyl ether.

SUMMARY

1. A saturated solution of cuprous chloride in hydrochloric acid (having a pH of 0.15 to 1.1) acts under determined conditions upon dimethylvinylcarbinol in such a manner than an allylic rearrangement and the dehydration of dimethylvinylcarbinol occurs with the formation of, in addition to isoprene and γ,γ-dimethylallylic alcohol two unsaturated ethers, γ,γ-dimethylallylic ether of 2-methyl-3-butene-2-ol (II) and γ,γ-dimethylallyl ether of 2-methyl-2-butene-4-ol (I).

2. A cleavage of the ether linkage occurred upon the catalytic hydrogenation of γ,γ-dimethylallylic ether of 2-methyl-3-butene-2-ol and γ,γ-dimethylallylic ether of 2-methyl-2-butene-4-ol at normal pressure and room temperature in the presence of platinum black with the formation of the corresponding amyl alcohols and the unsaturated hydrocarbon, isopentane.

3. The hydrogenation does not occur selectively under the given conditions. Simultaneously with the addition of the hydrogen to the double bond, occurs the cleavage of the ether linkage, and the formation of compounds containing a hydroxyl.

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INVESTIGATION OF COMPOUNDS CONTAINING A THREE MEMBERED OXIDE RING

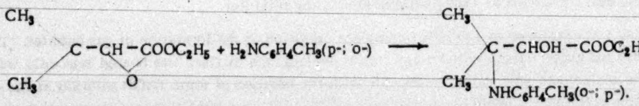
V. REACTION OF ETHYL β,β'-DIMETHYLGLYCIDATE WITH o- AND p- TOLUIDINE

V. F. Martynov

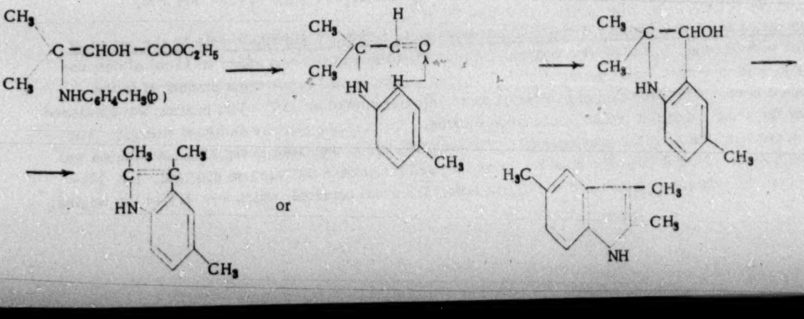
In the previous communication it was shown that the addition of aniline to ethyl β,β'-dimethylglycidate occurs with the formation of ethyl α-hydroxy-β-anilinoisovalerate. This means that the opening of the oxide ring of glycidic acid by the action of an aromatic amine occurs at the side of the β-carbon atom.

In view of the fact that these results were found to be in opposition to those of other authors [1], it was decided to prove the correctness of these conclusions upon other examples. For this purpose, the structures of the products of the reaction of o- and p-toluidine with ethyl β,β'-dimethylglycidate were investigated. The above products were obtained by the heating of ethyl β,β'-dimethylglycidate with the corresponding amine in sealed tubes at 150-180°. It was shown experimentally that the addition of p-toluidine to the oxide ring occurs comparatively easily; a 6 hour heating at the above temperatures led to a 60% yield of ethyl hydroxy-p-toluidine-isovalerate. o-Toluidine added with much greater difficulty. Upon heating the reaction mixture for the same 6 hours, the reaction product was obtained only in a 26% yield. Apparently, such a low yield can be explained by steric hindrances caused by the methyl group of o-toluidine. The reaction time was increased to 30 hours and as a result, a 50% yield of ethyl hydroxy-o-toluidineisovalerate was obtained.

The position of the cleavage of the oxide ring in the glycidic acid chosen, as in the previous cases, was determined by location of the hydroxyl group in the molecule. It could be readily expected that both the isomeric toluidines in this case should behave similarly to aniline, i.e., would form the amino derivatives of α-hydroxyisovaleric acid.


CH$_3$
C − CH − COOC$_2$H$_5$ + H$_2$NC$_6$H$_4$CH$_3$(p-; o-)
CH$_3$
O
CH$_3$
C − CHOH − COOC$_2$H$_5$
CH$_3$
NHC$_6$H$_4$CH$_3$(o-; p-).

Actually, both of the addition products obtained decarboxylated with the evolution of carbon dioxide by the action of concentrated sulfuric acid at 110-140°. This undoubtedly indicated that amino derivatives of α-hydroxyacids were being dealt with. For final solution of this problem, only the isolation of the decarboxylation products remained, which should be trimethyl indoles. This conclusion was possible on the basis of the investigated case of the decarboxylation of ethyl α-hydroxy-β-anilinoisovalerate where the product of the decarboxylation was 2,3-dimethylindole. Since in the given case toluidine, not aniline, was the starting material, the following must have been obtained: 2,3,5-trimethylindole from ethyl α-hydroxy-β-(p-toluidino)isovalerate, and 2,3,7-trimethylindole from ethyl α-hydroxy-β-(o-toluidino)isovalerate. The reaction of their formation can be described in the following manner on the example of 2,3,5-trimethylindole:



Indeed, upon making the acidic solution alkaline after the decarboxylation, the expected trimethylindoles were obtained which corresponded in analysis and melting point (individually and as the picrates) to the literature data. 2,3,5-Trimethylindole was isolated from the alkaline solution by steam distillation and was obtained in an 87% yield. 2,3,7-Trimethylindole was only distillable in small amounts with steam, and for this reason, it was extracted with ether from the alkaline solution; its yield was only 41% of the theoretical.

Such a great difference in the yields of the isomeric trimethylindoles, evidently, is explained by their different chemical stability. This difference, by the way, was apparent even during their storage. 2,3,5-Trimethylindole was stable; it only yellowed slightly upon 2-3 months standing in the air; 2,3,7-trimethylindole, on the other hand, darkened after a few days. Evidently, 2,3,7-trimethylindole is subjected more readily to the disruptive action of sulfuric acid than 2,3,5-trimethylindole; for this reason its yield was considerably smaller.

EXPERIMENTAL

Preparation of ethyl α-hydroxy-β-(p-toluidino)isovalerate. 13 g of p-toluidine and 20 g of ethyl β,β'-dimethylglycidate (the glycidic ester was used in excess in order to more completely use the p-toluidine) were sealed into a glass ampoule which was heated for 6 hours at 150-170°. The contents of the tube darkened slightly; there was no pressure when the tube was opened. The reaction mixture was vacuum distilled. The expected product distilled at 186-188° at 15 mm. It was a viscous, straw-yellow liquid. Weight 17.8 g, which was 60% of the theoretical based on the p-toluidine. After one day, the substance crystallized; after recrystallization from aqueous alcohol, it melted at 54-55°.

0.0229 g substance: 1.12 ml N_2 (17°, 755 mm). 0.02105 g substance: 1.08 ml N_2 (18°, 755 mm).

Found %: N 5.3, 5.6; $C_{14}H_{21}O_3N$. Calculated %: N 5.57.

The conversion of ethyl α-hydroxy β-(p-toluidino)isovalerate into 2,3,5-trimethylindole by the action of concentrated sulfuric acid. 2 g of ethyl α-hydroxy β-(p-toluidino)isovalerate was added to 10 ml strong sulfuric acid. Upon heating the mixture on an open electric hot plate, the substance dissolved, and the evolution of carbon dioxide started at 110° (thermometer in the mixture).

The heating was continued to 140° until complete cessation of the formation of gas bubbles. The mixture assumed a dark red color. Then, without any initial cooling, the mixture was poured into cold water with ice. The acid was neutralized with sodium carbonate with the addition of some NaOH solution at the end to a clearly alkaline reaction A white crystalline precipitate of 2,3,5-trimethylindole separated during the neutralization of the solution, which was steam distilled. 1.1 g of a colorless crystalline product with an unpleasant fecal odor was obtained. After recrystallization from dilute ethyl alcohol, the m.p. was 118-119°. The picrate, red-brown needles, m.p. 177-180°.

Found %: N 9.05. $C_{11}H_{13}N$. Calculated %: N 8.8. Literature data: melting point of 2,3,5-trimethylindole, 121.5°. Picrate, red brown needles, m.p. 177-180° [2].

Preparation of ethyl α-hydroxy-β-(o-toluidino)isovalerate. 15 g of ethyl β,β'-dimethylglycidate and 55 g of o-toluidine were sealed into a thick-walled tube and were heated for 30 hours at 170-180°. A slight pressure was present upon opening the tube. 15 g of a viscous straw-yellow liquid was isolated upon vacuum distillation. B.p. 134-135° at 2 mm. Yield 50 %.

d_4^{14} 1.0868; n_D^{14} 1.529; MR_D 71.23; Calculated 71.29.

0.2046 g substance: 12 ml N_2 (23°, 764 mm). 0.1805 g substance: 9.2 ml N_2 (23° 764 mm).
Found %: N 5.62, 5.74. $C_{14}H_{21}O_3N$. Calculated %: N 5.57.

Conversion of ethyl-α-hydroxy-β-(o-toluidino)-isovalerate into 2,3,7-trimethylindole by the action of concentrated sulfuric acid. 5 g of ethyl α-hydroxy-β-(o-toluidino)-isovalerate was added to 15 ml of concentrated sulfuric acid in a small round-bottom flask. The mixture was heated in the same manner as in the previous experiment. The evolution of bubbles of carbon dioxide started at 110°. The heating was continued to 140° until the cessation of the evolution of carbon dioxide. The reaction mixture darkened strongly. The subsequent procedure was as in the previous case. The emulsion which separated in the alkaline solution was extracted with ether. After drying, the ether was removed, and the residue was vacuum distilled. B.p. 105-106° at 2 mm. The substance crystallized in the exit tube. 1.3 g was obtained, which was 41% of the original yield. M.p. 86-87°. The picrate, red-brown crystals with m.p. 149-150°.

Found %: N 8.9. $C_{11}H_{13}N$. Calculated %: N 8.8.

Literature data: melting point of 2,3,7-trimethylindole, 79°. Picrate, m.p. 152° [3].

SUMMARY

1. The reaction between ethyl β,β'-dimethylglycidate and o- and p-toluidine was investigated. It was shown that the rupture of ring of the glycidic acid occurred at the site of the β-carbon atom by the action of both aromatic amines with the formation of nitrogen-substituted α-hyroxyisovaleric acids.

2. The conversion of ethyl α-hydroxy-β-(p-toluidino)isovalerate into 2,3,5-trimethylindole was accomplished; while 2,3,7-trimethylindole was obtained from ethyl α-hydroxy-β-(o-toluidino)isovalerate.

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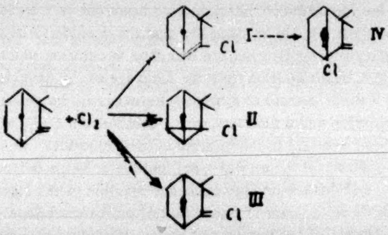
NEW TYPES OF TERPENE TRANSFORMATIONS

XIV. REACTION OF CHLORINE WITH CAMPHENE

D. Tishchenko

In communication I[1] general ideas were stated on the possible rules of the reaction of chlorine with terpenes, and predictions were given relative to the main direction of the reaction in each separate case and to the structure of the monochloroterpenes. For all cases studied up to now, without exception, these predictions were confirmed. They were also confirmed for the case of the reaction of chlorine with camphene. The sparse literature on the action of chlorine on camphene, reported in the same communication, gave no accurate description of the primary products of this reaction. For this reason, the prediction could only be proved experimentally. It was suggested that the "anomalous" reaction of M. D. Lvov must, for the case of camphene, be of less importance than for other terpenes, that camphene must be a "prohibited,' system (Bredt's Rule), and that this reaction may proceed in three different directions.

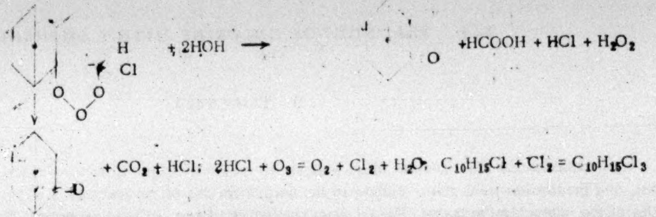


The degree of the "anomalous" reaction for camphene was found to be equal to 53-56 % which is considerably lower than the corresponding value for other terpenes; camphene monochloride is a mixture of the above three chlorides (I), (II), and (III). It is possible that chloride (IV) was present in small amounts in this mixture, but its presence was not proved beyond any doubt. The saturated camphene dichloride (product of the "classical reaction") was found to be a solid. Its structure did not follow the "rule of the smallest change in structure", which will be reported upon.

The mixture of monochlorides boiled within one degree. This fact alone indicated that the chlorine atom was structurally equivalent in all of these, and as it will be shown below, primary. As is known, secondary chloroterpenes boil 10-12° lower than the corresponding primary chlorides[2]. The investigation of this mixture posed very great difficulties, which were not unexpected. The structure of camphene proposed by Wagner, has been subject to doubts for more than thirty years because not even one transformation of camphene occurs uniformly, but always in different directions and is accompanied by isomerization. Even ozonolysis of camphene gives two products, camphenilone and a lactone. It was necessary to overcome the greatest difficulties during the investigation of the mixture of the three camphene monochlorides, to encounter many very unexpected results which did not have any analogy in chemical literature (see ozonolysis of one of the chlorocamphenes), and to study a series of transformations in order to come to a satisfactory conclusion by comparison of the results.

Initially, it was necessary to separate the mixture of chlorides, or the study of the transformations would have been senseless. The separation was accomplished by an exchange reaction with potassium acetate. The amount of active chlorine in the mixture of chlorides varied from 36-38% of the total. The chlorine at the double bond in chloride (III) must be inactive, the chlorine in chloride (II), a homolog of neopentyl chloride, must be only slightly active. The chlorides with the inert chlorine, (II) and (III) were separated by this conversion from the camphene acetate, a derivative of chloride (I). It was necessary to assume that the structure of camphenol corresponded to that of chloride (I), which was confirmed; camphenol was found to be primary.

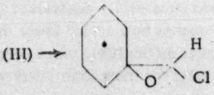
The ozonolysis of the chloride with the inactive chlorine consisting, as was finally shown, mainly of chloride (III) gave very surprising results. It was expected that camphenilone, hydrogen chloride, and formic acid would be obtained in equimolecular amounts.


H
Cl
O
O
O
+ 2HOH →
O
+HCOOH + HCl + H_2O_2
O
+ CO_2 + HCl; $2HCl + O_3 = O_2 + Cl_2 + H_2O$; $C_{10}H_{15}Cl + Cl_2 = C_{10}H_{15}Cl_3$

Actually, only 30% of the theoretical yield of camphenilone was obtained upon ozonolysis of chloroform or acetic acid, and only 15% of hydrogen chloride. In addition to camphenilone, a widely boiling mixture of other products was obtained, which contained chlorine, from which a crystalline trichloride of composition $C_{10}H_{15}Cl_3$ could be isolated. This trichloride was readily volatile, and for this reason was mixed with all fractions boiling lower than camphenilone, and did not allow them to be obtained in pure form. A lactone was also present, which was detected by titration with hot alkali, but could not be isolated pure. The same amounts of camphenilone and trichloride were also obtained upon ozonolysis of the inert chlorocamphenes in a mixture of glacial acetic acid and acetic anhydride, followed by decomposition of the ozonide by heating the solution to boiling, removing the solvents, and distilling the residue. This shows that the formation of the trichloride is not due to the cleavage of the ozonide by water, and occurs at the time of the ozonolysis. It can be suggested that the ozonide splits into camphenilone, carbon dioxide, and hydrogen chloride; the latter is partially oxidized by ozone to chlorine, which then adds to chloride (III) to form the trichloride $C_{10}H_{15}Cl_3$. The aqueous solution from the cleavage of the ozonide with water gave a qualitative reaction for formaldehyde, and a small amount of dimidone formal could be obtained from it. One of the higher boiling fractions contains the trichloride and a substance of the composition $C_9H_{13}OCl$. These two facts are proof of the possibility of the presence of chloride (IV) in the mixture of inert chlorides. At first glance, the chlorine in chloride (IV) appears strange (tertiary chlorides of the allylic type), but the chlorine is found at the carbon atom which stands at the head of a triple bridge. For this reason, any exchange reaction of the chlorine, occurring usually with a Walden inversion, is only possible in the case of the rupture of one of the bridge carbon atoms, which requires a very high energy of activation. Examples of the inertness of such tertiary chlorides are known [3]. Since only camphenilone, isolated in only 30% of the possible quantity, is an undoubted derivative of chloride (III), and the formation of the trichloride of unknown structure cannot be assigned to any known chlorocamphene, it was necessary to recognize that the method of ozonolysis did not prove the theory in the given case, because of the unexpected side reactions, and that it was necessary to search for some other transformation giving more definite products in better yield.

Similar results were given by the method of preparing oxides from a mixture of inert chlorides by the action of benzoyl hydroperoxide in chloroform solution.

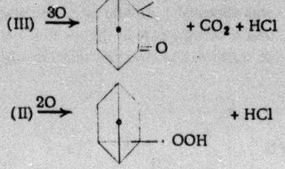
Part of the chlorides did not react (actually chloride (II)); a crystalline substance of composition $C_{10}H_{15}OCl$ was obtained in about 35% yield based on the reacted chloride. In addition, a complex mixture of high boiling products was obtained in the same yield as the camphenilone, and was a substance of unestablished structure; further study of this transformation and its products was not made.



An attempt to obtain primary oxidation products from the mixture of inert camphene chlorides by an insufficient amount of potassium permanganate in aqueous suspension, or in acetone solution was also unsuccessful. In spite of great variations in experimental conditions, the main part of the chlorides was recovered, while the oxidized part appeared as a mixture of extensively oxidized products which did not allow a clear-cut conclusion on the contents of any chlorocamphenes in the starting mixture. For this reason, the corresponding experiments are not reported in the experimental section.

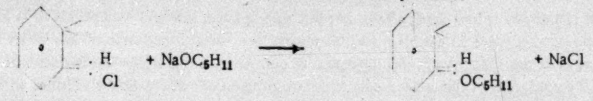
The best results were given by the oxidation of the inert chloride in 80% acetic acid by an excess of dry potassium permanganate. About 60% of the possible yield of camphenilone and 10% of dehydrocamphenilic acid were obtained with a consumption of about 10 g-atoms of active oxygen.

The products obtained require a very much smaller oxygen consumption. For this reason it must be recognized that there is another chloride in the mixture in addition to chlorides (III) (camphenilone is not oxidized by permanganate), and (II), which is oxidized much more extensively, or that part of dehydrocamphenylic acid was subjected to more extensive oxidation.

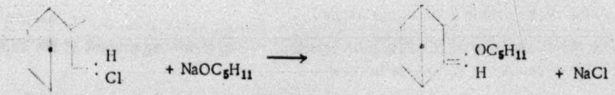


The same results on the amount of chloride (III) in the mixture were obtained by the study of the action of sodium amylate in isoamyl alcohol on the inert chlorocamphenes. Upon boiling the chlorides with sodium isoamylate in isoamyl alcohol, 67% of the chlorine was mineralized after 23 hours, and the reaction then stopped. 31% of the starting chloride, and 44%, based on the chloride reacted, of the isoamyl enol ether of camphenilanic aldehyde were found in the reaction products.

a)



b)



The ether gave upon hydrolysis with 3% hydrochloric acid, isoamyl alcohol and camphenilanic aldehyde, which was oxidized to isocamphenilanic acid with m.p. 117° by permanganate.

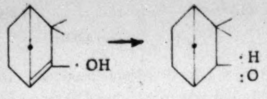
A semicarbazone was obtained from camphenilanic aldehyde which melted at 192-193° after two recrystallizations from alcohol. Henderson [4] gives an m. p. 191-192°. However, these results are untrue. Continued recrystallization of the above preparation from alcohol-benzene raised it to 207-208° after 4 recrystallizations; it did not change upon subsequent recrystallization from other solvents.

The chlorocamphene recovered from heating with sodium isoamylate was ozonized. Camphenilone was obtained in about 30% of the possible yield. This fact can be explained because chloride (III) was a mixture of cis and trans forms b and a, of which form a reacts with sodium isoamylate at lower temperatures (absence of steric hindrance from the side of the gem dimethyl group), than form b. In this case, the recovered chloride (form b) must react with sodium isoamylate at higher temperatures, which was confirmed experimentally. 70% of the chloride reacted in 5 hours at 210° in a sealed tube. 50% of the isoamyl camphenilic ether, based on the chloride reacted, was obtained. The total yield of the ether from forms a and b was slightly more than 60%. Therefore, the mixture of inert chlorides contains not less than 60% of chloride (III), which agreed with the results of the oxidation.

The presence of chloride (II) in the mixture was established by another method. It was stated above that, during the oxidation of the inert camphene chloride by a permanganate solution, the main part of the chloride was recovered. It was oxidized many times until the chloride began to be oxidized very slowly by permanganate solution. This chloride was converted into an organosodium compound by treatment with powdered sodium in isopentane, and was decomposed with water. The hydrocarbon obtained (b. p. 151-154) melted at 36-42°; it was purified from contaminants by Lipp's method [5]; it then melted at 58-68°. Camphene melts at 50°; tricyclene at 68°.

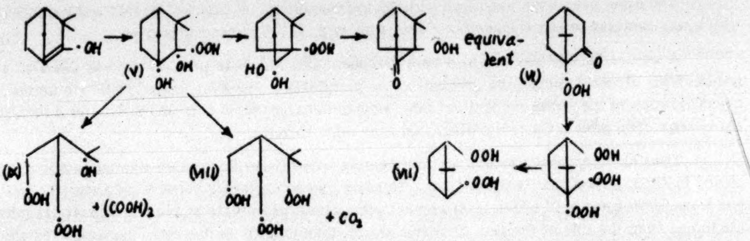
The structure of the chlorocamphene with the active chlorine, as stated above, had to be determined by means of the camphenol obtained from it, since the mixture of chlorides boiled within 1° and could not be separated by physical methods. Chlorides (II) and (III) were primary; for this reason, it could be assumed that chloride (I) was primary, and the chlorine atom in it bound to the same carbon atom in the isocamphene skeleton as in chlorides (II) and (III). Its acetate, obtained by the reaction with potassium acetate with the initial mixture of chlorides, boiled within 1°, its molecular refractivity, MRD (54.89) was somewhat greater than that calculated for the formula $C_{10}H_{15}OCOCH_3$ F (54.40). The ester was completely saponified only after a 6 hour boiling with alcoholic alkali which agreed with the structure (I) (sterically hindered). The alcohol obtained by the saponification of the ester was solid and homogenous, melted at 59-60°; it formed an acid phthalate melting at 142-143° on boiling with phthalic anhydride in benzene; therefore, the alcohol was primary. This fact leads to the conclusion that its structure corresponds to that of chloride (I) (primary). The acid phthalate was not obtained quantitatively by the reaction of equimolecular amounts of the alcohol and phthalic anhydride in boiling benzene. Simultaneously there was obtained a diphthalate, resulting in the formation of water which hydrolyzed the phthalic anhydride to the acid, and a certain part of the alcohol isomerized into an aldehyde (or mixture of aldehydes). Upon the deliberate addition of water to the reaction mixture, the aldehyde could be obtained in considerable yield. Its semicarbazone could be separated into poorly and readily soluble parts by crystallization from alcohol. The first part was brought to a constant m.p. 205-207° by recrystallization from alcoholic-benzene. A mixed melting point with camphenilanic aldehyde semicarbazone (see above) gave no depression. The readily soluble part was brought to a m.p. 148-149° by recrystallization from benzene. It was not determined to what aldehyde the last semicarbazone corresponded. The isomerization of the alcohol is in complete agreement with structure (I') and is analogous to that of allylic alcohol to propionaldehyde.

(I')



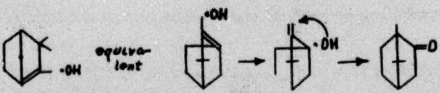
Structure (I) and (I') do not follow Bredt's rule, but this rule is not a law and exceptions to it are known [6]. In alcohol (I'), the double bond is found in the ring; for this reason, the careful oxidation of any of its esters with subsequent saponification must result in the neutral substance of composition $C_{10}H_{16}O_3$, which does not show an aldehydic reaction. By the oxidation of the sodium salt of the acid phthalate of the above alcohol with aqueous permanganate (2 gram atoms of oxygen), this substance was obtained in a yield of 40% of the possible, which confirmed the presence of a cyclic double bond in this alcohol.

A more extensive oxidation of alcohol (I') can be described by the following scheme if the experimentally established oxidation course of camphene [7] is kept in mind.



In this diagram, oxidation of the alcohol (I') accompanied by an intermediate pinacolin rearrangement, yields ketopinic acid (VI) and cis-apocamphoric acid (VII), while without the rearrangement it yields isocamphoric acid (VIII), a hydroxydicarboxylic acid (IX), and oxalic acid. Oxidizing isocamphenol in aqueous solution with an excess of potassium permanganate yielded cis-apocamphoric acid and its anhydride, isocamphoronic acid, oxalic acid, and acetic acid. About one-third of a mole of acetic acid was recovered per mole of camphenol. When camphenol was oxidized with a lesser quantity of permanganate, we got ketopinic acid. These experimental findings fully agreed with the suggested scheme for the oxidation of camphenol, which enables us to adopt the structure (I') for it with adequate certainty. What was unexpected was the securing of a small quantity of acetic acid, which is not oxidizable by permanganate, as we know. Its formation may be explained by the dehydration of the hydroxy isopropyl group of the unseparated acid (IX) to an isopropenyl group followed by the latter's oxidation. We were wholly unable to confirm this hypothesis, however.

The camphenol (I') is extremely easily soluble in all organic solvents, which made it difficult to recrystallize it to secure a constant melting point (59-60°). This was accomplished from aqueous methanol chilled to −20°. When we tried to recrystallize it from 70% acetic acid, in which it is moderately soluble, we found that the melting point rose with each successive crystallization, finally coming to a stop at 176-178°. A sample of camphenol with a m.p. of 59-60°, kept for 2 years in a not-tightly-sealed bottle in a draft where strong acids were present, exhibited a broad melting range (about 120-140°); recrystallizing it from acetic acid yielded crystals with a m.p. of 176-178°, which smelled of camphor and "skittered" over the surface of the water like camphor. A sample of these two specimens, mixed with inactive camphor (m.p. 176-178°) exhibited no depression of the melting point, so that they may be regarded as camphor. The isomerization of camphenol to camphor may be represented as follows, if we adopt its structure as (I'):



Therefore, the action of comparatively weak acids in low concentration isomerizes camphenol (I') into camphenilanic aldehyde, it is transformed into camphor by the action of comparatively weak acids in high concentration, or strong acids at low concentration.

EXPERIMENTAL

Chlorination of Camphene

The chlorination of camphene was conducted under previously (see previous communication) reported conditions with the only difference being that carbon tetrachloride was added in an amount necessary for the solution of the camphene. Isomerized camphene, filtered at 30-35° with m.p. 47-49°, was used. A report of one of these experiments is given below.

Camphene 350 g, CCl_4 150 g, $NaHCO_3$ 200 g, $KMnO_4$ 100 g, HCl (1.19) 750 ml. The chlorine in the chlorides after the removal of the CCl_4 and part of the camphene, 78.9 g, in salts, 31.1 g; yield of the "anomalous" reaction, 56%.

The CCl_4 and part of camphene were removed in water pump vacuum, the remaining camphene and the monochlorides were distilled through a herringbone, of 4-5 plates at 2 mm. Used initially: camphene 350 g, chlorine 110 g, total 460 g. Obtained: camphene 126 g, fraction 60-61° 128 g, crystalline residue 130 g, chloride ion 31 g, total 415 g; loss (camphene) 45 g.

Fraction 60-61° at 2 mm; d_4^{20} 1.009; n_D^{20} 1.4944.

Found %: Cl 20.4, 20.3. $C_{10}H_{15}Cl$. Calculated %: Cl 20.7.

The amount of active chlorine was determined by a 4 hour boiling with potassium acetate in acetic acid, and was equal to 36.5% of the total amount of chlorine.

The crystalline part was recrystallized from alcohol until the melting point remained unchanged at 134.5-135°. The substance was readily soluble in gasoline, benzene, acetone, ether, less in cold alcohol. It did not react with bromine water or permanganate solution.

Found %: Cl 34.5, 34.4. $C_{10}H_{16}Cl_2$. Calculated %: Cl 34.3.

Separation of the Monochlorides

330 g of monochlorides containing 35.0% of active chlorine of the total amount was heated to boiling in 500 ml of acetic acid with 200 g of potassium acetate for 8 hours. 53 g of KCl precipitated; the reaction had occurred completely. The acetic acid was distilled through a branched column in a water pump vacuum, the residue was diluted to 1 liter with water, extracted with ether, the ether was removed from the extracts, the residue distilled through an 8-10 plate column at 1 mm. These fractions were obtained: 1) up to 53°—5 g, 2) 53-54°—204 g, 3) 54-73°—5 g, 4) 73-74°—87 g, 5) 73-190°—10 g, residue 5 g, loss 28 g (in acetic acid).

Fraction 2: d_4^{20} 1.018; n_D^{20} 1.49245; MR_D 48.65; calculated 48.38.

Found %: Cl 20.6, 20.7, weight of bound chlorine. $C_{10}H_{15}Cl$. Calculated %: Cl 20.7.

Fraction 4: d_4^{20} 0.991; n_D^{20} 1.4731; MR_D 54.89; calculated 54.40.

Found saponification No. 284, 286. $C_{10}H_{15}OCOCH_3$. Calculated saponification No. 288.

Ozonolysis of Inert Monochlorides

5% by weight of ozone was passed into a solution of 34 g of the chloride in 100 ml of chloroform until saturation of the double bond. The ozonide solution was dropped into boiling water, the volatiles were steam distilled, the chloroform layer was distilled separately; the chloroform was removed and the residue (29.5 g) was distilled at 3 mm through a 6-8 plate column. The following fractions were obtained 1) to 56°—1.3 g, 2) 56-67°—9.0 g, 3) 58-80°—2.8 g, 4) 80-106°—4.0 g, 5) 106-130°—10.0 g, residue 2.0 g.

Fraction 2: d_4^{20} 0.998; n_D^{20} 1.4785. Found %: Cl 6.1 and 6.3.

The fraction solidified at −20°, the crystals were filtered and dried on a porous plate; m.p. 36-37°; camphoric odor.

Found %: C 77.9; H 10.1. $C_9H_{14}O$. Calculated %: C 78.2; H 10.1.

The substance was camphenilone. An oxime was prepared which was recrystallized to a constant m.p. 105-105.5° corresponding to camphenilone oxime.*

Fractions 3 and 4 were combined and distilled through a micro column. 1.8 g of a fraction with b.p. 70-72° at 1.5 mm was obtained; d_4^{14} 1.105.

Found %: C 63.0, 63.3; H 7.7, 7.9; Cl 20.1, 20.0. $C_9H_{13}OCl$. Calculated %: C 62.8; H 7.5; Cl 10.5.

In other experiments on the ozonolysis, this fraction of the chloroketone could not be isolated in such pure form; it contained more chlorine, less carbon, but if it was assumed that the fraction consisted of the chloroketone, and the trichloride $C_{10}H_{15}Cl_3$, and the amount of trichloride was calculated by means of the excess chlorine content, a satisfactory agreement of the analytical data with the calculated was obtained.

Fraction 5 was titrated with normal alkali while heated on the boiling water bath (it did not titrate in the cold, lactone type of neutralization). The insoluble part semisolidified on cooling. The crystals were filtered (1.8 g) and recrystallized from alcohol until a constant m.p. 127-128° was obtained. The substance did not react with bromine and permanganate solutions.

Found %: Cl 44.2, 44.6. $C_{10}H_{15}Cl_3$. Calculated %: Cl 44.2.

Amount of chlorine initially in fraction 5: Found 26.7-26.5%.

In the water in the distillation flask and the aqueous layer formaldehyde was detected qualitatively (fuchsine sulfurous acid + 0.1 N HCl, preparation of formal dimidone with m.p. 186-189°), and 0.958g Cl' was found, i.e. 13.6% of the total amount. The yield of camphenilone was about 21%.

32 - 35% of camphenilone could be obtained in other ozonolysis experiments in solutions in acetic acid and acetic anhydride, but the yield of hydrogen chloride was always about half. The trichloride was always obtained.

Preparation of Chlorocamphene Oxide

40 g of chlorides, 28 g of benzoyl hydroperoxide, 800 ml of chloroform. Parallel blank experiment. End of reaction after 72 hours. The acids in solution were neutralized with dilute alkali, the chloroform removed, the residue (37.5 g) distilled at 3 mm through a 6-8 plate column. The following fractions were obtained: 1) 64-65° −14 g, 2) 65-85°−2 g, 3) 85-90°−11 g (fraction crystallized), 4) 90-120°−2 g, 5) 120-180°−3 g, residue 1.3 g.

Fraction 3: Found %: Cl 18.9, 18.9. $C_{10}H_{15}OCl$. Calculated %: Cl 19.0.

The crystals were pressed on paper; m.p. 90-110°; they half melted in an open beaker with the evolution of HCl within 24 hours.

Oxidation of the Inert Camphene Chlorides

105 g of $KMnO_4$ was added stepwise with stirring to 40 g of the chloride in 400 ml of acetic acid and 100 ml of water; it heated spontaneously to boiling. After filtration, the light rose solution was steam distilled until the distillate no longer clouded upon dilution with water. The distillate was extracted three times with equal volumes of light gasoline (20-40°), the gasoline was removed from the extracts, and the residue (13.8 g) was distilled through a microcolumn at 23 mm. The following fractions were obtained 1) to 86°−0.5 g, 2) 86-90°−9.5 g, 3) 90-130° −0.5 g, 4) 130-150°−1.5 g, residue 0.5 g.

Fraction 2 solidified completely in the receiver; m.p. 36-37°. The oxime prepared from it melted at 105-106° after the first recrystallization from alcohol. The melting point did not change upon subsequent recrystallization. The substance was camphenilone.

Fraction 4 and the residue also crystallized. The crystals were pressed on a porous plate and recrystallized from aqueous alcohol to a constant m.p. 150-151°. The gram equivalent found was 166. The acid was dehydrocamphenilic.

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* Literature references are not given if the data are given in Beilstein's Handbook.

Reaction of Sodium Isoamylate with the Inert Chlorocamphene.

87 g of the chloride was heated to boiling with a solution of 16 g of sodium in 250 ml of isoamyl alcohol. NaCl separated and the alkalinity of the solution decreased gradually (titration of an aliquot with acid); after 23 hours the reaction ended; the alkalinity did not decrease any more. According to the alkali consumption, 67% of chlorine was mineralized. The reaction product and the amyl alcohol were steam distilled until no more of an oil came over. 0.347g-equiv. of mineralized chlorine was found in the distillation flask; the same as by consumption of alkali. The amyl alcohol layer was distilled through a 6-8 plate column at 6 mm. After the removal of the alcohol, the following were obtained: 1) 73-75°—31.3 g, 2) 75-90°—2.0 g, 3) 90-92°—8.2 g, 4) 92-123° —2.7 g, 5) 123-125°—33.8 g, residue 6.1 g.

Fraction 1 (d_4^{20} 0.996; Cl % 19.6 and 19.4) was camphene chloride.

Fraction 5 d_4^{20} 0.917; n_D^{20} 1.4800.

Found %: C 80.4, 80.6; H 11.8, 11.8. $C_{15}H_{26}O$. Calculated %: C 81.08; H 11.7.

15 g of the fraction and 300 ml of 3% HCl were distilled from a flask through a branched column until no more oil distilled. The distillate was extracted with ether, the ether was removed from the extracts, and the residue (14.0 g) distilled: 1) 126-132°—3.0 g, 2) to 79° at 6 mm—0.8 g, 3) 79-82°—5.5 g, 4) 82-130°—4.2 g, residue 1.2 g.

Fraction 1: d_4^{14} 0.816; n_C^{14} 1.4124 had the odor of isoamyl alcohol.

Fraction 3 solidified in the receiver; the crystals, pressed on a plate, melted at 65-69° (camphenilanic aldehyde melts at 68-70°). A semicarbazone was obtained from these which was taken to a m.p. 207-208° (See above). 1 g of the crystals was oxidized with aqueous permanganate. The acid obtained melted at 108-112° without recrystallization; after the first and second recrystallization from hot water, the m.p. was 117° as necessary for isocamphenilanic acid.

Found: g-equiv. 169; % C 71.5; H 9.8. $C_{10}H_{16}O_2$. Calculated: g-equiv., 168; % C71.4, H 9.5.

The chlorocamphene which did not react with sodium amylate, was ozonized. 32% of crystalline camphenilone with m.p. 35-37° was obtained; m.p. of the oxime, 106-106.5°.

30 g of the same chlorocamphene was sealed into two tubes with a solution of 4.6 g of sodium in 100 ml of isoamyl alcohol and was heated for 5 hours at 205-210°. The contents of the tubes was poured into water, 4.12 g of chloride ion was found in it corresponding to 70% of the chlorine in the chlorides. The oily layer was distilled at 12 mm. 14.3 g of a fraction 128-131° was obtained: d_4^{22} 0.916; n_D^{22} 1.4729. 12 g of the fraction was distilled with 300 ml of 3% of hydrochloric acid. The following were obtained: isoamyl alcohol, and camphenilanic aldehyde with m.p. 63-67°, which was oxidized to isocamphenilanic acid with m.p. 117°.

Preparation of Tricyclene from the Inert Camphene Chloride

14.4 g of the chloride recovered from several subsequent experiments with insufficient amounts of permanganate (not reported), were dropped with stirring onto 14 g of powdered sodium covered with isopentane. A spontaneous evolution of heat occurred, and the solvent boiled. Upon cooling, the solution of the organo-sodium compound was poured from the excess sodium and NaCl, and decomposed with water. The pentane layer was separated and distilled. 3.8 g of a solid hydrocarbon with b.p. 151-154° and m.p. 36-42° was obtained. The substance was oxidized with permanganate in acetic acid to a stable rose color, steam distilled, the crystals on the distillate were pressed on a paper (very volatile), dried over potassium hydroxide. M.p. 58-68° which corresponded to somewhat impure tricyclene.

Saponification of Camphenol Acetate

110 g of the ester (for constants see above) was saponified by a 6 hour boiling with 60 g of KOH in 200 ml of alcohol, the solution diluted with three volumes of water, and extracted with isopentane. The solvent was removed from the extract, the residue distilled at 11 mm. 80 g of a solid camphenol, b.p. 104-105° and m.p. 43-56° was obtained. It was very readily soluble in the usual solvents. It was recrystallized from 80% methanol with cooling to −20° until a constant m.p. of 59.5-60°. With less saponification time, the alcohol was obtained as a liquid because of impurities of the ester. It was recrystallized from alcohol and analyzed.

Found %: C 79.1, 79.0; H 10.5, 10.7: OH (Chugaev-Tserevitinov) 11.7, 11.2. $C_{10}H_{16}O$. Calculated %: C 78.9; H 10.4; OH 11.2.

Preparation of Camphenol Acid Phthalate

66 g of camphenol with m.p. 43-56°, 66 g of freshly sublimed phthalic anhydride, and 300 ml dry benzene were

heated to boiling for 2 hours. Water droplets collected from time to time in the condenser and were removed by wiping with filter paper. After the solution cooled, 25 g of phthalic anhydride crystals (g-equiv. found 67.6) precipitated. The benzene was removed, and the residue was dissolved in 300 ml of gasoline with heating (70-100°). Upon cooling to −23°, 55 g of the acid phthalate with m.p. 137-141° came out. The solvent was removed from the mother liquor through a column on the boiling water bath, using a water pump vacuum, and the residue was dissolved in 100 ml of gasoline. 12 g more of the phthalate with m.p. 135-139° came out at −23°. The gasoline was removed from the solution, and 1 g of a mobile liquid giving an aldehyde reaction was distilled from the substance on the water bath at 0.02 mm and up to 60°, and at 60-62° 18.7 g of camphenol melting at 46-52°, without recrystallization. Weight of the residue, 21.5 g; it was dissolved in 100 ml of hot gasoline. The gasoline was removed in vacuum from the mother liquor; weight of the final residue, 14.0 g (see below). Weight of products, 133.5 g; no losses. 16 g of recovered camphenol was heated for 15 hours to boiling with 16 g of phthalic anhydride The benzene was completely removed in vacuum at the end. The residue was dissolved in 200 ml of boiling gasoline, and 2.0 g of phthalic anhydride was filtered off (g-equiv. 83.6). Upon cooling of the solution, 24 g of an acid phthalate with m.p. 135-138° came out. All four residues were recrystallized from gasoline with very small losses to constant melting point, alone and in mixtures, of 142-143°. Light, fluffy needles which caused violent sneezing upon entering the nose. G-equiv. found 301. Calculated for $C_{10}H_{15}-OOC-C_6H_4-COOH$ 300.. Camphenol was homogeneous and primary [8].

The usual method for the isolation of the phthalate from the benzene solution did not apply in this case. Upon treatment of the solution with sodium carbonate, a colloidal, opalescent solution of benzene in the aqueous solution of the sodium salt of the phthalate was obtained. This phenomenon is known under the name of "hydrotropy", and is mentioned for many salts of organic acids.

14 g of the final residue was dissolved in ether, and treated with an excess of sodium hydroxide solution; 2 g dissolved. The ether was removed; weight of the neutral viscous substance, 12.0 g. It distilled almost completely at 146° and 0.08 mm. The saponification of 10 g of this fraction with alcoholic alkali gave 3.5 g of phthalic acid, isolated in the form of the potassium salt which was difficultly soluble in alcohol, and 6.0 g of camphenol with b.p. 100-101° at 9 mm and m.p. 46-54° (without recrystallization). An acid phthalate was obtained from the camphenol with m.p. 142-143° alone and mixed with the previous samples.

Isomerization of Camphenol into the Aldehyde

In one experiment on the preparation of camphenol acid phthalate from 69 g of the alcohol, 2-3 ml of water fell into the reaction flask because of a poorly fitted reflux condenser. The contents of the flask were heated to boiling for 12 hours. Upon cooling, 16 g of phthalic acid crystallized. The benzene solution was distilled. The residue did not crystallize upon the removal of the benzene; it was a mobile liquid with a strong individual odor different from that of camphenol, resembling that of camphor. It was distilled through a 6-8 plate column at 17 mm. 36 g of a fraction with b.p. 88-89° was obtained.

d_4^{24} 0.9525; n_D^{21} 1.4676; MR_D (for aldehyde $C_{10}H_{16}O$) found 44.33; calculated 44.0.

The substance gave all of the qualitative tests for aldehydes. 6 g of the fraction was heated for 1 hour to boiling with 4.5 g of semicarbazide acetate in 50 ml of alcohol, half of the alcohol was distilled off, and the residue diluted with four times as much water. A solid precipitated which was separated by means of alcohol into difficultly (2.2 g) and very readily (2.0 g) soluble parts. Recrystallization of the first part from alcoholic benzene, and the second from benzene, led to constant m.p.'s of 205-207°, and 148-149°, respectively. The first semicarbazone melted without depression when mixed with solid camphenilanic aldehyde semicarbazone (m.p. 207-208°). See the general section for the isomerization of camphenol into camphor.

Oxidation of Camphenol Acid Phthalate in the Neutral Substance $C_{10}H_{16}O_3$

13.5 g of the phthalate was dissolved in 300 ml of water and 5 g of $NaHCO_3$, and 10 g of $KMnO_4$ in 500 ml of water was added dropwise with cooling and stirring to the solution; the MnO_2 was filtered, the filtrate was acidified, and extracted with ether. The ether was removed from the extracts; weight of the residue, 15.2 g; it was saponified by a 2 hour boiling with 110 ml of normal alkali. The water was removed in vacuum from the solution, and the solid residue was extracted 4 times with 100 ml of acetone with rubbing. The acetone was removed from the extracts; weight of the semi-solid residue, 4.6 g. It did not distill, but sublimed at 0.1 mm; 3.5 g of a solid sublimate was obtained in a sabre flask and 0.9 g of a residue. The sublimate was recrystallized from benzene; fine, dense crystals with m.p. 169-170°

Found %: C 65.3, 65.5; H 8.9, 8.8. $C_{10}H_{16}O_3$. Calculated %: C 65.3; H 8.7.

The substance did not give an aldehyde reaction; it evidently was a diketoalcohol.

Oxidation of camphenol leading to ketopinic acid

1400 ml of a 4% permanganate solution was added with stirring and heating to 75° on a bath, to 10 g of camphenol suspended in 100 ml of water. The manganese dioxide was filtered, leached twice with 1/2 liter of boiling water, the combined filtrates evaporated to 50 ml, and acidified to Congo with hydrochloric acid, d 1.10. The precipitated potassium chloride was filtered, and washed with ether; the filtrate was extracted four times with ether, and the ether removed from the extracts; weight of the viscous residue, 11 g. It was dissolved in alcohol, and four volumes of benzene were added to the solution; 0.55 g of crystals deposited. They were recrystallized from hot water; clusters of thin prisms; m.p. 230-232°.

Found %: C 65.2; H 7.6; g-equiv. 186. $C_{10}H_{14}O_3$ (ketopinic acid). Calculated %: C 65.9; H 7.4; g-equiv. 182. Ketopinic acid melts at 233.5-234.5°.

Extensive oxidation of camphenol

32 g of camphenol in a liter of water (flask with reflux condenser and stirrer) was oxidized with stirring and heating (toward the end at 75°) with dry permanganate added slowly until a stable rose color (180 g). The manganese dioxide was filtered, leached four times with a liter of boiling water, the combined filtrates distilled to 300 ml, the distillate and residue extracted four times with ether, and the ether removed from the extracts; weight of the residue (neutral substances), 0.6 g; it was not investigated. The alkaline residue (300 ml) was acidified to Congo with hydrochloric acid, and the carbon dioxide collected in a gasometer (3950 ml). The acidic solution was steam distilled to a neutral distillate; amount of volatile acids, calculated as acetic, 4.07 g. The distillate was neutralized with sodium hydroxide, evaporated, the salt fused, weight, 5.7 g; 5.7 g of sodium acetate was expected. Part of the salt was converted to the silver salt; its silver content amounted to 64.6%, corresponding to that of acetic acid. One tenth of the acid solution from the distilling flask was saturated with an excess of calcium chloride, the precipitate was filtered, washed, and dried at 170°; wt. 0.170 g. Found %: CaO 43.6. C_2O_4Ca. Calculated %: CaO 43.7.

The remaining acid solution was extracted three times with equal volumes of ether, the ether was removed from the extracts; weight of the viscous residue, 14 g (acid I). The aqueous layer was evaporated until the start of salt crystallization; it was filtered, washed with a small amount of cold water, the combined filtrates extracted three times with ether, and the ether removed from the extracts; weight of the viscous residue, 5.3 g (acid II). The aqueous layer was slowly evaporated along with the filtered mineral salts; weight of the viscous residue, 11.0 g; it was insoluble in acetone; upon combustion, an alkali salt remained. 5 ml of fuming hydrochloric acid was added to it, and the reaction product was extracted with ether 3 hours later. 7.3 g (acid III) was extracted.

Acid I did not crystallize after 3 weeks. 6.4 g of a substance was sublimed from a saber flask at a bath temperature of 160-180° and 1.10^{-4} mm; weight of the residue, 5.7 g; loss 2.5 g. The sublimate was dissolved in acetone, benzene was added dropwise to it until a cloudiness formed. 1.2 g of crystals deposited; they were recrystallized to a constant m.p. 208-209° (small cubes).

Found %: C 58.3; H 7.8; g-equiv. 93.5. $C_9H_{14}O_4$. (Cis-apocamphoric acid, m.p. 206-208°).
Calculated %: C 58.1; H 7.5; g-equiv 93.0.

The acetone-benzene mother liquor was evaporated to dryness, the residue dissolved in gasoline, and poured in a crystallizer. Growths of needles surrounded by an oil appeared as the gasoline evaporated. They were pressed on paper and recrystallized from gasoline to an m.p. 175-176°. The substance was not titrated by alkalies in the cold; it could be titrated while boiling; g-equiv. 84.8 g. Cis-apocamphoric acid anhydride melts at 176°, g-equiv. 84. The substance was dissolved in alkali, the solution was acidified to Congo with hydrochloric acid, and poured into a crystallizer. Four days layer, cubes of cis-apocamphoric acid with m.p. 208-209° and g-equiv. 93.3 were obtained.

Acid II solidified after 60 days into a slurry of crystals surrounded by a viscous liquid. They were spread on a porous plate and placed into a desiccator with 10 ml of ether A white powder remained on the plate (3.2 g) with m.p 160-172° and g-equiv. 72.3. It was recrystallized to a constant m.p. 166-167°.

Found %: C 49.2; H 6.5; g-equiv 72.6. $C_9H_{14}O_6$ (isocamphoric acid, m.p. 166-167°). Calculated %: C 49.5; H 6.4; g-equiv 7.27.

Acid III did not crystallize in 90 days. It was dissolved in ether, gasoline was added, the solution poured into a crystallizer. Crystals surrounded by an oil appeared as the gasoline evaporated. The crystals, 2.2 g, were filtered, dissolved in 10 ml of water, and allowed to stand in an open beaker. Two weeks later, crystals deposited. M.p. 164-166°, g-equiv. found 71.1 – isocamphoric acid.

SUMMARY

1. The action of chlorine on camphene was studied. In contrast to all other terpenes, three monochlorides were formed as primary products: ω-chlorocamphene (III), 7-chlorotricyclene (II) and bicyclo [1,2,2]-3-chloromethyl-2,2-dimethylheptene-3 (I); the latter was formed in opposition to Bredt's rule. The possibility of the formation of these chlorides was suggested in communication I.

2. The extent of the "anomalous" reaction was lower than with other terpenes (~ 55%); saturated dichlorocamphene was formed in a yield of about 40%.

3. The following were obtained by ozonolysis of chloride III, independent of the conditions of ozonolysis and decomposition of the ozonide: camphenilone (~ 30%), hydrogen chloride (~ 15%), and a saturated trichloride $C_{10}H_{15}Cl_3$. There is no analogy in the literature for the formation of the trichloride.

4. Chloride (I) was almost quantitatively saponified (via the acetate) into the corresponding terpenol (I'). The latter could be isomerized into camphenilanic aldehyde, as well as into camphor.

5. Chloride (III) was a mixture of cis and trans forms reacting at various temperatures with sodium amylate to form the amyl enol ether of camphenilanic aldehyde. Camphenilanic aldehyde semicarbazone had m.p. 206-207°, and not 191-192° [4].

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* See Consultants Bureau Translation, page. 593.

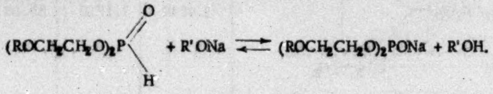
** See Consultants Bureau Translation, page 931.

REACTION OF DIALKYLPHOSPHORIC ACIDS WITH ALDEHYDES AND KETONES

V. β-METHOXYETHYL AND β-ETHOXYETHYL ESTERS OF α-HYDROXYALKYLPHOSPHINIC ACIDS

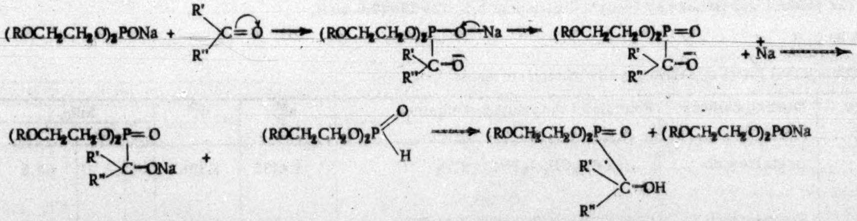
V. S. Abramov, Yu. A. Bochkova, and A. D. Polyakova

In the previous communications [1] it was shown that dialkylphosphoric acids reacted with aldehydes and ketones. The reaction occurs in the presence of freshly prepared alkali metal alcoholates. The methyl, ethyl, propyl, and other α-hydroxyalkylphosphinic esters were reported on in the previous papers. The present communication reports on the β-methoxyethyl and β-ethoxyethyl esters of α-hydroxyalkylphosphinic acids. The above esters are obtained by the reaction of di-β-methoxyethylphosphoric and di-β-ethoxyethylphosphoric acids with various aldehydes and ketones the reaction, as in the previously reported cases, occurs in the presence of small amounts of alkali metal alcoholates, in particular, sodium methylate. The reaction proceeds rapidly with a great evolution of heat. By analogy to other dialkylphosphoric acids, the mechanism for this reaction can be represented by the following scheme. Sodium alcoholate reacts with di-β-methoxyethylphosphoric acid or di-β-ethoxyethylphosphoric acid to form their sodium salts.



$$(ROCH_2CH_2O)_2P\overset{O}{\underset{H}{<}} + R'ONa \rightleftharpoons (ROCH_2CH_2O)_2PONa + R'OH.$$

The carbon of the carbonyl group becomes cationic during the reactions because of the shift of electrons, and interacts with the lone pair of electrons on the phosphorus of the sodium salt of the di-β-alkoxyethylphosphoric acid.



and etc., where R is CH_3 and C_2H_5, and R' and R", the various radicals of the aldehydes and ketones.

As a result of the reaction, β-methoxyethyl and β-ethoxyethyl esters of α-hydroxyalkylphosphinic acids are formed in accordance with this scheme.

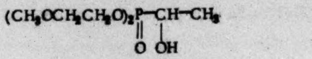
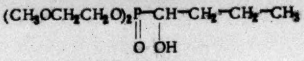
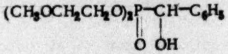
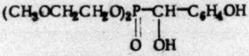
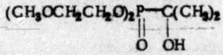
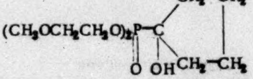
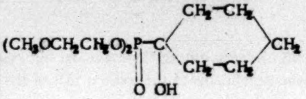
The esters obtained are transparent, syrupy liquids, very often immobile, according to their physical properties.

An attempt to purify the esters obtained by vacuum distillation at 2 mm was unsuccessful. The esters decomposed into the starting materials during distillation. Only the product of the reaction between di-β-methoxyethylphosphoric and di-β-ethoxyethylphosphoric acid and acetone distills with partial decomposition. For this reason it was necessary to choose other methods of purification. The purification of β-methoxymethyl and β-ethoxyethyl-α-hydroxyalkylphosphinic esters was effected by adsorption in simple systems. Fused aluminum oxide and activated charcoal in series served as the adsorbants. Methanol served as the solvent, and in several cases benzene was used. A list of the esters obtained and their constants are given in the Table.

The reaction was also effected with other carbonyl compounds: methylethyl ketone, methylpropyl ketone, acetophenone, benzophenone, benzil, and others. The corresponding β-methoxyethyl and β-ethoxyethyl esters of the α-hydroxyalkylphosphinic acids could not be isolated. Increase in temperature and change in physical properties of the mixture during the experiment indicated that a reaction between these substances had occurred.

TABLE 1

β-Methoxyethyl Esters of α-Hydroxyalkylphosphinic acids

Expt. No.	Starting carbonyl compound	Formula of the substance obtained	n_D^{20}	d_4^{20}	MR_D	
					Found	Calc.
1	Acetaldehyde . .	 $(CH_3OCH_2CH_2O)_2\underset{O}{\underset{\Vert}{P}}-\underset{OH}{\underset{\vert}{CH}}-CH_3$	1.4401	1.1681	54.61	54.31
2	Butyraldehyde . .	 $(CH_3OCH_2CH_2O)_2\underset{O}{\underset{\Vert}{P}}-\underset{OH}{\underset{\vert}{CH}}-CH_2-CH_2-CH_3$	1.4466	1.1365	63.49	63.55
3	Benzaldehyde . .	 $(CH_3OCH_2CH_2O)_2\underset{O}{\underset{\Vert}{P}}-\underset{OH}{\underset{\vert}{CH}}-C_6H_5$	1.5055	1.2241	73.7	73.8
4	Salicylaldehyde .	 $(CH_3OCH_2CH_2O)_2\underset{O}{\underset{\Vert}{P}}-\underset{OH}{\underset{\vert}{CH}}-C_6H_4OH$	1.4975	—	—	—
5	Acetone	 $(CH_3OCH_2CH_2O)_2\underset{O}{\underset{\Vert}{P}}-\underset{OH}{\underset{\vert}{C}}(CH_3)_2$	1.4365	1.1540	57.97	57.83
5a*	Acetone		1.4345	1.1573	57.67	—
6	Cyclopentanone .		1.4640	1.1910	65.43	65.96
7	Cyclohexanone . .		1.4660	1.1648	70.37	70.5

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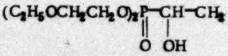
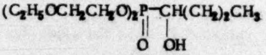
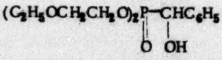
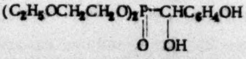
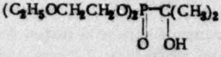
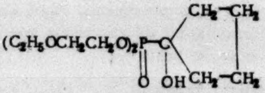
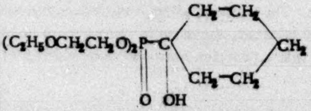
* The product was isolated by vacuum distillation; b.p. 125-126°(2.5 mm).

TABLE 2

β-Ethoxyethyl Esters of α-Hydroxyalkylphosphinic Acids

Expt. No.	Starting carbonyl compound	Formula of the substance obtained	n_D^{20}	d_4^{20}	MR_D	
					Found	Calc.
1	Acetaldehyde . .	 $(C_2H_5OCH_2CH_2O)_2\underset{O}{\underset{\Vert}{P}}-\underset{OH}{\underset{\vert}{CH}}-CH_3$	1.4430	1.128	63.5	63.5
2	Butyraldehyde . .	 $(C_2H_5OCH_2CH_2O)_2\underset{O}{\underset{\Vert}{P}}-\underset{OH}{\underset{\vert}{CH}}(CH_2)_2CH_3$	1.4476	1.100	72.5	72.7
3	Benzaldehyde. . .	 $(C_2H_5OCH_2CH_2O)_2\underset{O}{\underset{\Vert}{P}}-\underset{OH}{\underset{\vert}{CH}}C_6H_5$	1.4988	1.188	82.0	83.0
4	Salicylaldehyde .	 $(C_2H_5OCH_2CH_2O)_2\underset{O}{\underset{\Vert}{P}}-\underset{OH}{\underset{\vert}{CH}}C_6H_4OH$	—	—	—	—
5	Acetone	 $(C_2H_5OCH_2CH_2O)_2\underset{O}{\underset{\Vert}{P}}-\underset{OH}{\underset{\vert}{C}}(CH_3)_2$ *	1.4410	1.097	68.3	68.2
6	Cyclopentanone		1.4570	1.135	75.7	75.2
7	Cyclohexanone		1.4562	1.110	79.4	79.8

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* B.p. 144-145° (2 mm).

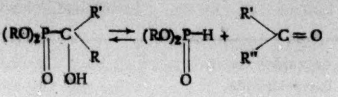
Table 1

Percent phosphorus		Yield (in % of the theoretical)
Found	Calc.	
12.61, 12.78	12.81	79.9
11.67, 11.64	11.48	60.6
10.53, 10.48	10.20	69.7
10.09, 10.00, 9.95	9.69	59.0
12.06, 12.09	12.11	66.4
—	—	—
11.35, 11.42	11.0	66.1
10.51, 10.55	10.47	55.8

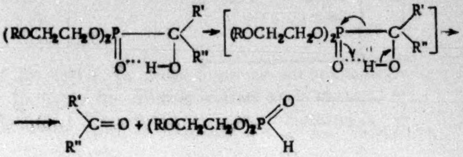
Table 2

Phosphorus content (%)		Yield (in % of the theoretical)
Found	Calculated	
11.7, 11.8	11.5	67.3
10.3, 10.5	10.4	53.1
10.3, 10.3	9.5	69.5
9.0, 9.1	8.9	50.7
10.8, 10.7	10.7	34.0
10.1, 10.2	10.0	53.0
10.5, 10.5	9.5	74.6

During the study of properties of esters of *α*-hydroxyalkylphosphinic acids it was shown [2], that a decomposition into the starting substances occurs during heating, and that the equilibrium is shifted toward the formation of the starting compounds with increase in temperature.



The ease of rupture of the C—P bond is explained by the presence of a hydroxy group in the *α*-position and the presence of a hydrogen bond within the ester molecules. With the above studied reaction between di-β-methoxyethylphosphoric and di-β-ethoxyethylphosphoric acids and the above ketones, evidently, an analogous decomposition process of the β-methoxyethyl and β-ethoxyethyl *α*-hydroxyalkylphosphinic esters which were formed, occurs at the C—P bond. The decomposition of the esters may be represented by the scheme:



where R is CH_3 and C_2H_5 and R' and R", the various radicals of the ketones.

For this reason it is clear why the corresponding esters of the *α*-hydroxyalkylphosphinic acids could not be isolated. Their decomposition occurs, apparently, so readily that the heat evolved during the reaction forming them leads to the reverse process. In other cases, evidently, it occurs during the process of purification by the heating. Decrease in the temperature at the time of the purification process in certain cases had a beneficial effect on the preparation of the corresponding esters, for example, during the reaction of di-β-methoxyethylphosphoric acid with cyclohexanone, butyraldehyde, and others. The choice of the temperature during the purification of the *α*-hydroxyalkylphosphinic esters is of great importance.

EXPERIMENTAL

The experiments were conducted in the following manner. Equimolecular mixtures of di-β-methoxyethylphosphoric, or di-β-ethoxyethylphosphoric acid, and the aldehyde or ketone were prepared, and a small amount of freshly prepared sodium methylate dropped into them. In order to control the course of the reaction, the temperature, refractive index, and the density of the equimolecular mixture of the reacting substances was determined before the addition of the sodium methylate; the sodium methylate was then added and a rise in temperature occurred; at the completion of the reaction

TABLE 3

Course of the Reaction Between Di-β-methoxyethylphosphoric Acid and Carbonyl Compounds

Expt. No.	Starting carbonyl compound	Amounts of the reacting substances		Constants of the starting mixture		Increase of temperature during the reaction		n_D^{20} of the mixture after reaction
		Carbonyl compound	Dialkyl-phosphoric acid	n_D^{20}	d_4^{20}	from	to	
1	Acetaldehyde	2.11	9.5	1.4287	1.085	24	80	1.4390
2	Butyraldehyde.	3.0	8.0	1.4241	1.044	26	111	1.4400
3	Benzaldehyde.	4.4	8.0	1.4775	1.133	19	64	1.4952
4	Salicylaldehyde	2.67	4.2	1.4880	1.167	24	48	1.4848
5	Acetone	4.2	12.0	1.4205	1.106	25	80	1.4315
6	Cyclopentanone	4.0	8.0	1.4337	1.080	16	47	–
7	Cyclohexanone	4.0	8.0	1.4372	1.079	26	87	1.4285
8	Methylethyl ketone* .	3.7	10.0	1.4203	1.074	22	66	1.4235
9	Methylpropyl ketone**	2.17	5.0	1.4190	1.031	21	49	1.4285
10	Acetophenone.	3.0	5.0	1.4775	1.095	28	57	1.4535
11	Benzophenone.	3.64	4.0	1.4970	1.139	18	91	1.4960
12	Dibenzyl ketone	4.36	4.0	1.4970	1.112	23	38	1.4975
13	Benzil 1:1	5.3	5.0	–	–	73	120	1.4975
14	Benzil 1:2***	9.0	18.8	1.4650	1.1606	24	66	1.4610

*Constants of the reaction product: d_4^{20} 1.1826; n_D^{20} 1.4625; MR_D 62.81; calculated 63.55.

** Constants of the reaction product: d_4^{20} 1.091; n_D^{20} 1.4220; MR_D 66.15; calculated 68.17.

*** Constants of the reaction product: d_4^{20} 1.1757; n_D^{20} 1.4625; MR_D 66.15; calculated 68.17.

TABLE 4

Course of the Reaction between Di-β-ethoxyethylphosphoric Acid and Carbonyl Compounds

Expt. No.	Starting carbonyl compound	Amounts of the reacting substances		Constants of the starting mixture		Increase of temperature during the reaction		n_D^{20} of the mixture after reaction
		Carbonyl compound	Dialkyl-phosphoric acid	n_D^{20}	d_4^{20}	from	to	
1	Acetaldehyde	2.4	12.0	1.4229	1.034	23	110	1.4390
2	Butyraldehyde.	2.8	9.1	1.4230	1.037	21	97	1.4404
3	Benzaldehyde.	2.1	4.5	1.4696	1.079	21	81	1.4937
4	Salicylaldehyde.	2.4	4.7	1.4844	1.119	25	79	1.4441
5	Acetone	3.0	9.1	–	–	20	72	–
6	Cyclohexanone.	2.1	4.5	1.4372	1.045	17	78	1.4562
7	Cyclopentanone	2.1	4.5	1.4330	1.043	16	65	1.4512
8	Methylethyl ketone. . . .	1.8	4.5	1.4150	0.997	18	66	1.4225
9	Methylpropyl ketone . .	1.3	3.5	1.4191	0.998	20	62	1.4245
10	Acetophenone.	1.8	4.5	1.4649	1.087	27	109	1.4460
11	Benzophenone.	3.6	4.5	1.4970	1.102	19	107	1.4956
12	Dibenzyl ketone	4.2	4.6	1.4964	1.083	22	40	1.4880
13	Benzil 1:2.	4.2	9.2	–	–	49	101	1.4828
14	Benzil 1:1.	4.2	4.6	–	–	63	116	1.4680

the constants were again determined. The purification of the product obtained was then effected.

The purification of the esters was conducted in the following manner. The reaction product was dissolved in 3-4 parts of methyl alcohol, the solution placed into a round bottom flask with a reflux condenser; 10-15 g freshly fused aluminum oxide was then added to the flask. The contents of the flask were heated on the water bath for 1-2 hours. The solution of the product was filtered from the aluminum oxide. Activated carbon was added to the filtrate and it was heated once more for 1-2 hours on the water bath. The carbon was filtered. The filtrate was placed into an Arbuzov flask, the solvent, methyl alcohol, distilled off in vacuum with slight heating. The carbonyl compounds were removed during this operation, if they had not been adsorbed. The constants for the residue were determined. The prepared β-methoxyethyl α-hydroxyalkylphosphinic esters are given in Table 1, and the β-ethoxyethyl hydroxyalkylphosphinic esters in Table 2.

The conditions for the reaction between di-β-methoxyethylphosphoric acid and di-β-ethoxyethylphosphoric acid and compounds containing a carbonyl group are given in Tables 3 and 4.

SUMMARY

1. Di-β-methoxyethylphosphoric and di-β-ethoxyethylphosphoric acid reacted with aldehydes and ketones in the presence of sodium methylate. As a result of the investigation conducted, seven new methoxyethyl and seven new ethoxyethyl esters of various α-hydroxyalkylphosphinic acids were prepared and characterized.

2. Reactions were conducted between di-β-methoxyethylphosphoric and di-β-ethoxyethylphosphoric acids and ketones such as acetophenone, benzophenone, and others. The reaction between them was confirmed by increase in the temperature; however, the corresponding esters of the α-hydroxyalkylphosphinic acids were not obtained, which was explained by the ease of rupture of the C–P bonds in these esters.

LITERATURE CITED

[1] V. S. Abramov, Proc. Acad. Sci. USSR, 73, 487 (1950); V. S. Abramov, J. Gen. Chem., 22, 647 (1952);* V. S. Abramov, R. V. Dmitrieva, and A. S. Kapustina, J. Gen. Chem., 23, 257 (1953). **

[2] V. S. Abramov, L. P. Semenova, and L. G. Semenova, Proc. Acad. Sci. USSR, 84, 281 (1952).

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* See Consultants Bureau Translation, p. 709.

** See Consultants Bureau Translation, p. 269.

REACTION OF BENZENE WITH ESTERS IN THE PRESENCE OF VARIOUS CATALYSTS

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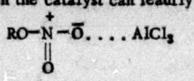
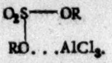
As the many literature results [1,2] and those of the authors' previous investigations [3,4] showed, esters can react with benzene in the presence of catalysts of the type $AlCl_3$ in two directions: 1) analogous to the alkyl halides, i.e., to form benzene homologs; 2) similar to acid halides, to form ketones in the case of carboxylic esters and nitro compounds in the case of nitrates, etc.

The presence of radicals readily split from oxygen, for example CH_3– and $C_6H_5CH_2$–, favors the alkylation reaction; with the phenyl radical, stably attached to the oxygen, acylation occurs. As for the acidic residue, then it can be thought that alkylation would occur more readily with esters of strong acids. However, esters of two strong acids, nitric and sulfuric, react differently with benzene. Benzene is nitrated by methyl and ethyl nitrate [5]; with dimethyl sulfate and diethyl sulfate, as was shown by one of the authors [3] and was confirmed by other investigators [6], only alkylation occurs. It is considered possible to explain this difference by the fact that the first stage of the process in both cases is complex formation between the ester and the catalyst with the complex formation occurring differently.

According to the rules of quantum mechanics and the results of physical and chemical investigations, the nitrogen in the so-called compounds with a pentavalent nitrogen is actually a tetravalent positive one. One of the bonds of nitrogen with oxygen in nitro compounds and the alkyl nitrates must be semi-polar. For this reason, the alkyl nitrate combines with the catalyst, primarily, because of the negative charge on the oxygen atom. Sulfur can be fully hexavalent. If the double bond between sulfur and oxygen in the dialkyl sulfate is covalent and not readily capable of forming complexes, then the catalyst can readily add to the ester oxygen as with ethers:



$$\mathrm{RO-\overset{+}{\underset{\underset{O}{\|}}{N}}-\bar{O}\ldots AlCl_3}$$



$$\begin{array}{l}\mathrm{O_2S-OR}\\ \ \ |\\ \mathrm{RO\ldots AlCl_3.}\end{array}$$

Upon the subsequent reaction with benzene, the nitrate complex is attracted to the carbon of the benzene ring with their nitrogen. This finally leads to the formation of nitrocompounds. The complexes of the sulfate type must react similarly to those of $AlCl_3$ with hydrocarbon halides or ethers, i.e., in the alkylation direction. Esters of carboxylic acids, evidently, are capable of forming complexes of both types, i.e., the ether of the carbonyl oxygen can participate.

The following problems were posed for the present investigation: 1) to study the reaction of benzene with a large number of different esters and catalysts; 2) to study the course of the reaction using smaller amounts of catalyst than is recommended according to the literature results; 3) to try to separate intermediate complexes between the esters and the catalyst, and benzene with the catalyst and the ester.

The experimental results agree with the above suggestion of two types of complex formation with esters and catalysts. Those esters which were expected to give complex formation resulting from the ether oxygen, gave alkyl benzenes. Esters of boric acid can react in both directions since complexes of the ester with the catalyst can give off alkyls, but boron can also add to the benzene ring. The latter was observed in the experiment with tributyl borate.

The assumed complex compound could not be isolated in experiments with ethyl nitrate. Evidently, for a detailed analysis of the course of the process fine physical methods must be applied, as for example, absorption spectra. However, an indirect proof of the formation of some sort of a complex compound with the ester and $SbCl_5$ was obtained. The latter itself readily chlorinates benzene. If ethyl nitrate is added initially to benzene, then the subsequent addition of $SbCl_5$ leads only to nitration. Evidently, $SbCl_5$ gives a product very rapidly with the nitrate which subsequently reacts with benzene to form nitrobenzene.

EXPERIMENTAL

In most of the experiments, the catalyst was added to 156 g of benzene (2 moles), and then the ester was added. In experiments with $SbCl_5$, it was necessary to initially mix the benzene with the ester, and then add the

Expt. No.	Esters	Moles (for 2 moles of C_6H_6)	Catalyst	Moles (for 2 moles of C_6H_6)	Products	Yield in % of the theoretical (based on the ester)
1	$C_2H_5ONO_2$	0.5	$AlCl_3$	0.25	$C_6H_5NO_2$	81
2	$C_2H_5ONO_2$	0.5	$ZnCl_2$	0.25	$C_6H_5NO_2$	0
3	$C_2H_5ONO_2$	0.5	$SnCl_4$	0.25	$C_6H_5NO_2$	29.6
4	$C_2H_5ONO_2$	0.5	$SbCl_5$	0.25	$C_6H_5NO_2$	49.2
5	$C_6H_5ONO_2$	0.226	$SbCl_5$	0.144	$C_6H_5NO_2$	83.6
6	$SO_2(OC_2H_5)_2$	0.5	$AlCl_3$	0.25	$C_6H_5C_2H_5$ $C_6H_4(C_2H_5)_2$	17 10.9
7	$SO_2(OC_2H_5)_2$	0.5	$FeCl_3$	0.25	The reaction did not occur	
8	$SO_2(OC_2H_5)_2$	0.5	$ZnCl_2$	0.25		
9	$SO_2(OC_2H_5)_2$	0.5	$SnCl_4$	0.25		
10	$SO_2(OC_2H_5)_2$	0.5	$SbCl_5$	0.25		
11	$SO_2(OC_2H_5)_2$	0.5	$BiCl_3$	0.125		
12	$PO(OC_2H_5)_2$	0.25	$AlCl_3$	0.25	$C_6H_5C_2H_5$	23
13	$B(OC_4H_9)_3$	0.5	$AlCl_3$	0.125	Boron organic compound	
14	$Si(OCH_3)_4$	0.17	$SnCl_4$	0.25	The reaction did not occur	
15	$Si(OC_2H_5)_4$	0.125	$AlCl_3$	0.125	$C_6H_5C_2H_5$	12
16	$CH_3COOC_2H_5$	0.125	$AlCl_3$	0.125	The reaction did not occur	
17	$CH_3COOC_2H_5$	0.125	$SbCl_5$	0.125		
18	$CH_3COOC_4H_9$	0.125	$ZnCl_2$	0.125		
19	$CH_3COOC_5H_{11}$	0.125	$AlCl_3$	0.125		
20	$CH_3COOCH_2C_6H_5$	0.125	$AlCl_3$	0.125	$C_6H_5CH_2C_6H_5$	70.7
21	$CH_3COOCH_2C_6H_5$	0.125	$AlCl_3$	0.125		79.0
22	$CH_3COOCH_2C_6H_5$	0.125	$CuCl_2$	0.125	The reaction did not occur	
23	$CH_3COOCH_2C_6H_5$	0.125	$ZnCl_2$	0.125		
24	$CH_3COOCH_2C_6H_5$	0.125	$ZnBr_2$	0.125		
25	$CH_3COOCH_2C_6H_5$	0.125	$SnCl_4$	0.125	$C_6H_5CH_2C_6H_5$	66.6
26	$CH_3COOCH_2C_6H_5$	0.125	$SbCl_5$	0.125	$C_6H_5CH_2C_6H_5$	36.0
27	$CH_3COOCH_2C_6H_5$	0.125	$BiCl_3$	0.125	$C_6H_5CH_2C_6H_5$	14.0
28	$CH_3COOCH_2C_6H_5$	0.125	AlI_3	0.125	The reaction did not occur	
29	$CH_3COOC_6H_5$	0.125	$AlCl_3$	0.125		11.2
30	$CH_3COOC_6H_5$	0.125	$SbCl_5$	0.125		
31	Triacetin	1/15	$AlCl_3$	0.2	$C_6H_5COCH_3$	28
32	Triacetin	1/15	$SbCl_5$	0.2	$C_6H_5COCH_3$	29
33	$CH_2ClCOOC_2H_5$	0.125	$AlCl_3$	0.125	$C_6H_5C_2H_5$	54.2
34	$CH_2ClCOOCH_3$	0.5	$AlCl_3$	0.125	The reaction did not occur	
35	$(CH_3)_2CBrCOOC_2H_5$ . . .	1/15	$AlCl_3$	1/15	$C_6H_5C_2H_5$	19.2
36	$CH_2CNCOOC_2H_5$	0.25	$AlCl_3$	0.125	$C_6H_5C_2H_5$	8.0
37	$CO(OCH_3)_2$.	0.125	$AlCl_3$	0.125	The reaction did not occur	
38	$COOC_2H_5COOC_2H_5$	0.125	$AlCl_3$	0.125	$C_6H_5C_2H_5$	15.4
39	$COOC_2H_5CH_2COOC_2H_5$.	0.125	$AlCl_3$	0.125	$C_6H_5C_2H_5$	12.5
40	$C_6H_5SO_2OCH_3$	0.125	$AlCl_3$	0.25	$C_6H_5CH_3$	32
41	$C_2H_5OC_2H_5$	0.5	$AlCl_3$	0.125	The reaction did not occur	
42	$C_2H_5OC_2H_5$	0.5	$SbCl_5$	0.125		
43	$C_5H_{11}OC_5H_{11}$	0.125	$AlCl_3$	0.125		
44	$(C_6H_5CH_2)_2O$	0.125	$AlCl_3$	0.125	$C_6H_5CH_2C_6H_5$	91.5
45	$(C_6H_5CH_2)_2O$	0.125	$SnCl_4$	0.125	$C_6H_5CH_2C_6H_5$	79.9
46	$(C_6H_5CH_2)_2O$	0.125	$SbCl_5$	0.125	$C_6H_5CH_2C_6H_5$	40.5

catalyst. If the reaction was violent, the mixture had to be cooled at first. Later it was heated for 6 hours on the water bath, water was then added, and sometimes acidified with HCl, and the reaction product was extracted with ether, or steam distilled. The ether-benzene, or benzene solution was dried and distilled through a dephlegmator. The experimental results are given in the Table.

Notes for the Individual Experiments

Nos. 1,3,4,5. Based on the amount of catalyst used, the yield of the product was 162, 59.2, 28.4, and 143%, respectively.

No. 6. The total percent ethylation was $17 + 10.9 \cdot 2 = 38.8\%$.

Nos. 12, 15, 33, 35, 36, 38, 39. Ethyl benzene was converted into acetophenone and its phenylhydrazone.

Nos. 31, 32. A phenylhydrazone with m.p. 104-105° was obtained from the reaction product.

No. 40. The toluene obtained gave 2,4-dinitrotoluene with m.p. 68° upon nitration.

SUMMARY

1. The reaction of benzene with many esters of organic and inorganic acids in the presence of a series of catalysts was studied. Supplementary results on the relation of the direction of the reaction to the nature of the ester and catalyst were obtained.

2. An explanation for the different course of the reaction is given, based on the assumption of different types of complex formation of the ester and the catalyst.

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IODINATION OF BENZOIC ACID AND BENZALDEHYDE IN THE PRESENCE OF A NITRIC-SULFURIC NITRATING MIXTURE

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Several methods have been suggested for the preparation of meta-iodobenzoic acid. It is obtained: 1) from benzoic acid by means of the nitro,amino, and diazo compounds; 2) from phthalamide by means of anthranilic and 5-iodoanthranilic acid; 3) by the direct iodination of benzoic acid with iodine in the presence of fuming nitric acid saturated with sulfur trioxide [3] in yields of 55%; from benzoic acid, iodine, concentrated sulfuric acid and silver sulfate [2] in yields of 75%.

The last method gives a good yield of the product but cannot be considered convenient since it requires a great consumption of the valuable reagent (Ag_2SO_4 is used in equimolecular amount with benzoic acid and iodine).

Recently a method of direct iodination in the presence of fuming nitric acid has entered laboratory practice [1] for the preparation of iodobenzene. In the author's laboratory fuming nitric acid was replaced by the usual nitrating mixture prepared from nitric acid of density 1.38-1.40. This method gave the same yield of C_6H_5I, with some changes in the conditions of conducting the experiments.

It was decided to apply an analogous method for the iodination of benzoic acid. A large number of experiments were conducted to determine the effect of the ratio of the amounts of benzoic acid, iodine, sulfuric, and nitric acids, the order of addition of the reagents, temperature, and reaction time. It was found that the addition of acetic acid as a solvent had a very beneficial effect, wherein it was found that 80% acetic acid was well as glacial could be used. The strong initial sublimation of iodine was very bothersome and led to a decreased yield and the soiling of the apparatus. A better medium for coping with the sublimation was found to be the addition of carbon tetrachloride. The vapors of the latter were condensed in the colder parts of the apparatus and the flowing CCl_4 returned the iodine to the reaction mixture. An inexpensive and simple method for the isolation and purification of the product was also developed. As a result, constant yields of 75% meta-iodobenzoic acid were achieved in the best experiments. The melting point and the results of the determination of the halogen, according to Stepanov, proved the purity of the acid. A qualitative test for nitrogen gave a negative result.

The same reaction was studied with benzaldehyde because of interest in the oxidizing action of nitric acid. The iodination of the aldehyde under the same conditions as were used with benzoic acid led only to the preparation of meta-iodobenzoic acid, but with a lower yield. Therefore, in addition to the iodination of the benzene ring, the oxidation of the aldehyde group to the carboxyl occurred. Since the greatest oxidative properties are possessed not by nitric acid, but by the nitrous acid and nitrous oxide formed from it, the iodination of benzaldehyde was conducted with the addition of urea. Meta-iodobenzaldehyde was obtained in yield up to 20%, which cannot be considered the maximum since the effect of various conditions on this process has not been sufficiently determined.

EXPERIMENTAL

Iodination of benzoic acid. The benzoic acid, iodine, solvents, and in certain experiments, sulfuric acid were mixed in a 200 ml three-necked flask with fittings for a condenser, dropping funnel, and stirrer with a seal. The mixture was heated to the desired temperature on a sulfuric acid bath (with thermoregulator). The nitric acid or a mixture with sulfuric acid was then added gradually with stirring. The heating was continued after the addition of the HNO_3. Crystals of iodobenzoic acid gradually formed in the homogenous liquid, nitrous oxide was evolved, and the liquid became lighter. The iodine subliming during the experiment was washed down with the carbon tetrachloride into the reaction mixture. The mixture was stirred from time to time.

At the end of the experiment, the mixture was transferred into a beaker, and the precipitate was washed into it with distilled water. More water was added to the beaker, and some more crystals precipitated. The crystals were then separated by filtration and washed, first with cold water, and then with hot. A mixture, evidently, of unreacted benzoic acid and iodobenzoic acid precipitated in the filtration flask. After washing, the product was recrystallized from aqueous alcohol (50%) 2 or 3 times. Meta iodobenzoic acid with m.p. 185-187° was obtained.

Found (according to Stepanov) %: I 50.6, 50.8. $C_7H_5O_2I$. Calculated %: I 51.17.

The results of the experiments are given in the Table.

Effect of Conditions on the Yield of Meta-Iodobenzoic Acid

Amount in moles				Amount (in ml)		Temperature	Time (in hours)	Yield (in % of the theoretical)
C_6H_5COOH	I_2	HNO_3	H_2SO_4	CH_3COOH	CCl_4			
0.15	0.075	0.6	0.6	50	–	125*	4	35.1
0.15	0.075	0.3	0.3	50	–	125	4	48.0
0.15	0.075	0.15	0.15	50	–	125	4	50.0
0.15	0.075	0.9	0.9	50	–	125	4	0
0.05	0.025	0.075	0.075	15	4	85	7	58.2
0.05	0.025	0.0625	0.0875	15	4	85	7	66.3
0.05	0.025	0.05	0.1	15	4	85	7	74.0
0.05	0.025	0.0375	0.1125	15	4	85	7	69.2
0.05	0.025	0.025	0.125	15	4	85	7	63.6
0.05	0.025	0.025	0.1	15	4	85	5	43.3
0.05	0.025	0.0375	0.1	15	4	85	5	51.3
0.05	0.025	0.05	0.1	15	4	85	5	66.0
0.05	0.025	0.1	0.1	15	4	85	5	67.5
0.05	0.025	0.15	0.1	15	4	85	5	68.2
0.05	0.025	0.05	0.05	15	4	85	5	14.0
0.05	0.025	0.05	0.075	15	4	85	5	42.5
0.05	0.025	0.05	0.1	15	4	85	5	65.0
0.05	0.025	0.05	0.125	15	4	85	5	60.1
0.05	0.025	0.05	0.15	15	4	85	5	55.8
0.05	0.025	0.075	0.075	15	4	75	4	38.5
0.05	0.025	0.075	0.075	15	4	85	4	56.2
0.05	0.025	0.075	0.075	15	4	100	4	46.0
0.05	0.025	0.075	0.075	15	4	125	4	24.5
0.05	0.025	0.05	0.1	15	4	85	2	36.1
0.05	0.025	0.05	0.1	15	4	85	3	58.5
0.05	0.025	0.05	0.1	15	4	85	4	63.0
0.05	0.025	0.05	0.1	15	4	85	5	65.0
0.05	0.025	0.05	0.1	15	4	85	6	69.4
0.05	0.025	0.05	0.1	15	4	85	7	74.0
0.05	0.025	0.05	0.1	15	4	85	8	71.6
0.5	0.25	0.562	1	150	40	85	7	75.3

Iodination of benzaldehyde. 10.1 ml of C_6H_5CHO, 12.69 g of iodine, 20.67 ml of HNO_3, and 16.71 H_2SO_4 were used. Temperature, 85°, experiment time 6 hours. Without acetic acid and urea, only benzoic acid was isolated; with 30 ml of glacial CH_3COOH, 51.3% of meta-iodobenzoic acid were obtained. 4.6 g (20%) of meta-iodobenzaldehyde with m.p. 58° was obtained in an experiment with 30 ml of CH_3COOH and 8 g urea. The phenylhydrazone obtained from the aldehyde had an m.p. 156°.

SUMMARY

1. A method for the synthesis of meta-iodobenzoic acid by the action of iodine on benzoic acid in the presence of a nitric sulfuric nitrating mixture was developed. A stable yield of not less than 75% of the theoretical was obtained. The given method is simpler and less expensive than the methods for the preparation of meta-iodobenzoic acid reported in the literature.

2. The suggested method is also applicable for the preparation of meta-iodobenzaldehyde. It is only necessary to add urea, without which the oxidation of the aldehyde group to the carboxyl occurs.

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CATALYTIC ALKYLATION OF ANILINE WITH ETHYL ALCOHOL

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The preparation of alkyl and dialkylanilines in the presence of aluminum oxide, thorium oxide, promoted aluminum oxide, and other oxide catalysts has been studied by a series of investigators [1]. The properties of natural aluminum silicate, bentonite was studied by one of the authors. It was shown that this clay, the main part of which is montmorillonite $Al_2O_3 \cdot 4SiO_2 \cdot nH_2O$, was a catalyst for the dehydration of alcohols [2] and for the simultaneous dehydration of alcohols and acid anhydrides [3]. Because of this fact it seemed of interest to determine whether it was possible to apply bentonite as a catalyst for the simultaneous dehydration of alcohols and aniline in order to obtain alkylanilines. It was shown that, at 350°, a molar ratio of aniline to ethyl alcohol of 1:2, and a volume velocity of 0.15, a yield of ethyl aniline up to 87-89% of the aniline reacted was obtained.

In addition, for the preparation of esters, activated carbon, soaked with phosphoric acid, conditionally called "solid phosphoric acid" later [4] was used. It was shown that in the presence of this catalyst, good yields of propyl and butyl acetates and butyrates are obtained by the mutual dehydration of alcohols and acids in the vapor phase. This made it possible to suppose that "solid phosphoric acid" could be used as dehydration catalyst for the reaction of aniline with alcohol.

In the present investigation it was shown that the alkylation of aniline with alcohol could be accomplished in the presence of "solid phosphoric acid" with the predominant formation of ethylaniline. The yield of ethylaniline at 275° volume velocity 0.3, and a molar ratio of aniline to alcohol of 1:2 to 1:5 was 59-62% of the aniline reacted.

EXPERIMENTAL

Experiments on the alkylation of aniline were conducted in a general apparatus for effecting reactions in the vapor phase by the flow method. The reaction mixture was prepared from freshly distilled, initially well dried aniline and ethyl alcohol. At the end of the experiment (for a better separation of the catalyzate) a stream of nitrogen was passed for 30-40 minutes. The catalyzate obtained consisted of two layers: an aqueous alcohol layer and an amine layer. The latter was thoroughly dried over fused potassium hydroxide and distilled. The fraction boiling up to 160° was discarded (unreacted alcohol and traces of aniline). The fraction, 160-235°, was subjected to further investigation, and consisted of unreacted aniline, ethylaniline, and diethylaniline.

The freshly distilled reaction product was analyzed by a method developed for the determination of primary amines in mixtures of amines [5].

The temperature, the ratio of components, and the rate of passage of the reaction mixture were varied in order to find the optimum conditions for the formation of ethylaniline over bentonite and "solid phosphoric acid".

Alkylation of Aniline in the Presence of Bentonite.

Commercial bentonite activated with sulfuric acid and preheated in a catalytic furnace to 400-430° was used for the reaction.

The effect of the temperature and the ratio of the reaction components on the yield of ethylaniline. A mixture of aniline and ethyl alcohol in molar ratios of 1:1, 1:1.5, 1:2, and 1:2.5 was used. The reaction mixture was passed over the catalyst at a constant velocity of 0.15 at temperatures of 350-450. At temperatures below 350° the alkylation reaction of aniline proceeded with small yields.

From the data given in Table 1, it follows that the largest yield of ethyl aniline occurs at 350° and ratios of aniline to alcohol of 1:1.5, 1:2. A further increase of the temperature and the concentration of the alcohol causes a gradual decrease in the yield of the alkylaniline. The catalyzate obtained distilled almost completely at 180-212°, and only a small amount distilled at a higher temperature (to 235°). This indicated that the alkylation product of aniline was ethylaniline, with a very small impurity of diethylaniline.

TABLE 1

Experiment temperature (in °C)	Percent of aniline transformed at ratios of aniline to alcohol of			
	1:1	1:1.5	1:2	1:2.5
350	80.7	86.5	87.2	81.2
375	77.5	79.5	80.4	77.9
400	73.2	73.7	74.3	74.0
425	67.8	71.0	72.2	69.9
450	64.1	66.3	70.5	67.5

TABLE 2

Experiment temperature (in °C)	Volume velocity	Percent aniline transformed
350	0.07	88.6
350	0.15	87.2
350	0.30	27.0

TABLE 3

Experiment temperature	200°	250°	275°	300°	350°	400°
Percent of aniline transformed at a ratio of reacting substances of 1:1	23.6	37.7	49.5	37.7	30.0	16.0
Percent of aniline transformed at a ratio of reacting substances of 1:1.5	38.6	53.6	58.6	52.0	26.7	21.0

TABLE 4

Composition of the catalyzate (in %)

Experiment temperature	250°	275°	300°
Aniline	46.4	41.4	48.0
Ethylaniline	47.8	54.4	48.7
Diethylaniline	5.8	4.2	3.3

Effect of the rate of the passage of the reaction mixture on the yield of ethylaniline. The following experiments were conducted as the above, at the passage of the mixture of aniline -alcohol with a volume velocity of 0.15. In order to determine the effect of the velocity of passage of the mixture on the yield of ethylaniline, the volume velocity was decreased to 0.07, and then increased to 0.30.

The results of the experiments are given in Table 2, from which it follows that the increase of the volume velocity from 0.07 to 0.15 has little effect on the yield of the ethylaniline upon alkylation of aniline over bentonite. Further increase of the velocity of passage of the reaction mixture to 0.30 causes a sharp decrease in the yield of ethylaniline.

Alkylation of Aniline in the Presence of "Solid Phosphoric Acid"

The catalyst used for this investigation was prepared by a method which was reported for the preparation of esters [4].

Effect of temperature on the yield of ethylaniline. Two series of experiments were set up: the first with a molar ratio of aniline to alcohol of 1:1, and the second with a ratio, 1:1.5.

The experiments were conducted at temperatures of 200-400° and volume velocity of passing the reaction mixture of 0.1. The results of these experiments are given in Table 3.

Diethylaniline, as well as aniline, was determined in the catalyzates obtained from experiments conducted at 250, 275, and 300° (Table 4).

On the basis of these experiments it can be concluded that:

1) the optimum temperature for the ethylation of aniline under these experimental conditions is 275° (Table 3); the decrease in the yield of ethylaniline with the further increase of the temperature was explained by the strong decomposition of the alcohol which was proved by special experiments;

2) ethylation reaction of aniline over the given catalyst proceeds mainly in the direction of the formation of ethylaniline; diethylaniline was obtained in small quantities, and its yield decreased with decreasing temperatures (Table 4).

TABLE 5

Volume velocity of the passage of the reaction mixture	0.1	0.3	0.6	1.0
Percent of aniline transformed	58.6	65.15	54.6	53.2

TABLE 6

Molar ratio of aniline : alcohol	1:1	1:1.5	1:2	1:4	1:5	1:6
Yield of crude catalyzate(in%)	82.5	80.0	80.0	75.0	68.9	60.7
Amount ethylaniline in the catalyzate(in %)	55.2	65.2	73.5	82.0	90.2	94.8
Yield ethylaniline on the aniline reacted (in %)	45.5	52.0	59.0	61.5	62.0	57.5

Effect of the velocity of passage of the reaction mixture on the yield of ethylaniline. The experiments were conducted at the optimum temperature of 275° and at a ratio of the components of 1:1.5; the volume velocity of the passage of the reaction mixture was varied from 0.1 to 1.0.

From the results given in Table 5, it follows that increasing the velocity of passage of the reaction mixture does not sharply affect the yield of ethylaniline; however, the best yield occurs at the passage of the mixture of aniline-alcohol with a volume velocity of 0.3.

Effect of the quantitative ratio of the reacting components on the yield of ethylaniline. In order to determine this effect, a series of experiments was set up with various mixtures in which the molar ratio of the aniline and the alcohol was varied from 1:1 to 1:6. All of the experiments in this series were conducted at 275° and a volume velocity of the passage of the mixture of 0.3. The results are given in Table 6.

From the results given in Table 6 it follows that the yield of ethylaniline in the catalyzate is 94-95% when there was a large excess of alcohol to the aniline (1:6), but a considerable part of the alcohol was decomposed to ethylene, which did not react; the yield of the catalyzate was only 60% under these conditions. For this reason the most satisfactory mixture of aniline and alcohol to use was a ratio of 1:2, with which the yield of the aniline in the catalyzate was somewhat lower, 73.5% but, based on the aniline reacted was almost always constant at 57.5-59%.

On the basis of the experiments conducted it can be considered completely established that "solid phosphoric acid" can be used satisfactorily for the alkylation reaction of aniline with ethyl alcohol.

SUMMARY

1. The catalysts employed in this investigation, bentonite and "solid phosphoric acid", caused mutual dehydration in the system aniline-alcohol. Ethylaniline is mainly formed as a result of this dehydration; diethylaniline is only formed in small amounts.

2. The optimum conditions for the preparation of ethylaniline over bentonite are 350°, a ratio of aniline to alcohol of 1:2, and a volume velocity of passing the reaction mixture of 0.15. Under these conditions, the yield of ethylaniline is 87% of the aniline reacted.

3. The optimum conditions for the preparation of ethylaniline over "solid phosphoric acid" are: 275°, ratio of aniline to alcohol of 1:2, and a volume velocity of passage of the reaction mixture of 0.3. Under these conditions, the yield of ethylaniline was 59% of the aniline reacted.

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INTRODUCTION OF A CARBOXYL GROUP INTO AROMATIC AMINES

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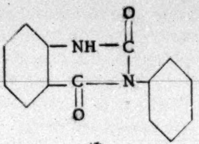
One of the authors showed that, by heating aromatic amines with carbon dioxide and alkali metal carbonates, or certain chlorides, the formation of very small amounts of amino carboxylic acids occurred. Thus if aniline was heated at 170-180° under CO_2 pressure in the presence of K_2CO_3, Na_2CO_3, or $CaCl_2$, o- and p-aminobenzoic acids could be isolated.

Upon further investigation, it was found that the amino carboxylic acids were obtained with relatively better results if N-acyl derivatives were used instead of the free aromatic amines [1,2]. The latter were heated with K_2CO_3 under CO_2 pressure to 185-260°. The maximum yield achieved was 25% of theory based on the amine used, and about 80% based on the amine recovered. o- and p-aminobenzoic acids were obtained from acetanilide, diphenylurea (symm.), benzanilide, and phenyl isocynate; from acet-p-toluidine, 3-methyl-6-aminobenzoic acid; from 3,3' dimethyldiphenylurea, 4-methyl-6-aminobenzoic acid; from 3,3'-dichlorodiphenylurea, 4-chloro-6-aminobenzoic acid; from acet-1-naphthylamine, 1,2- and 1,4-naphthylamine carboxylic acid.

o-Aminocarboxylic acids were obtained at the end of the reaction to a great extent in the form of derivatives of 2,4-dioxotetrahydroquinazoline.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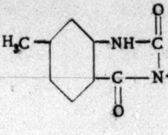
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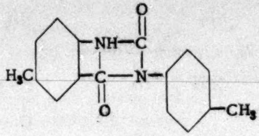
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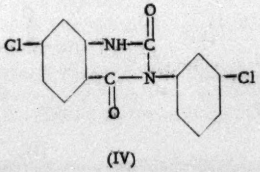
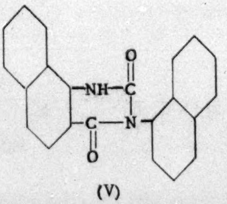
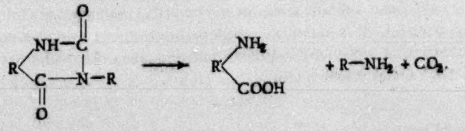

(IV)


(V)

The latter are cleaved into the corresponding o-aminocarboxylic acids and amines by heating for several hours with 5-10% solutions of alkalies.

(A)

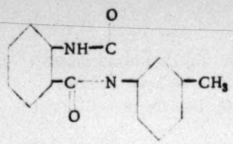


The formation of derivatives of 2,4-dioxotetrahydroquinazoline during the process of heating N-acylamines with K_2CO_3 under CO_2 pressure only became comprehensible when it was found that these compounds can be obtained by heating salts of o-aminocarboxylic acids under CO_2 pressure. Thus (I) was obtained from potassium anthranilate, and (III), from potassium p-toluidine-o-carboxylate.

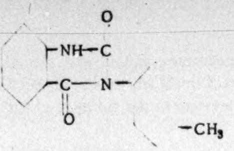
Since a partial decarboxylation always occurs during the heating of salts of o-aminocarboxylic acids, and amines are formed, the conversion of o-aminocarboxylic acids into derivatives of 2,4-dioxotetrahydroquinazoline can be represented by a scheme which is the reverse of scheme (A).

If this scheme is correct, the formation of various 2,4-dioxotetrahydroquinazolines could be expected upon heating salts of o-aminocarboxylic acid with various amines.

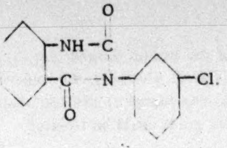
Actually, heating, for example, potassium anthranilate under CO_2 pressure with m-toluidine, p-toluidine, and m-chloroaniline resulted in the following, respectively:



(VI)



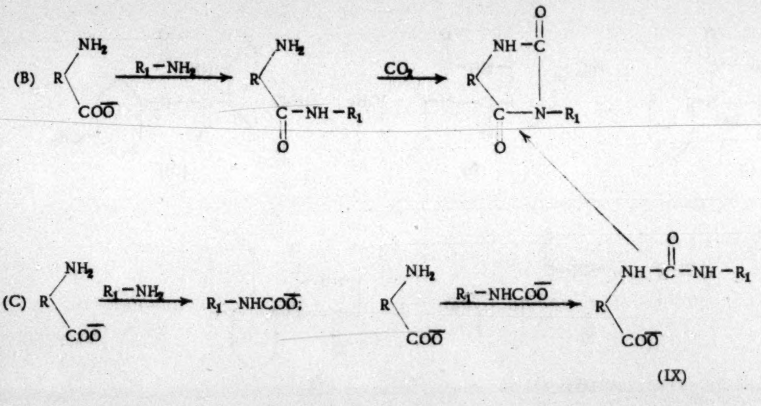
(VII)



(VIII)

Several compounds of this type are reported in the literature; they are obtained by the condensation of o-aminocarboxylic acids with amines which contain a carbonyl group on the nitrogen. Derivatives of urea and the corresponding isocyanates [3] are equivalent to such amines.

The preparation of derivatives of 2,4-dioxtetrahydroquinazoline from salts of o-aminocarboxylic acids under CO_2 pressure appeared possible by the aid of one of the following schemes:



(IX)

A test of scheme (B) gave negative results. The formation of quinazoline derivatives did not occur when the anilide of anthranilic acid was heated under CO_2 pressure.

The isolation of product (IX) would have been a direct proof for scheme (C). Attempts to isolate (IX) however, as it could be expected, were unsuccessful. It is known that anthranilides of aryl amino-N-carbamic acids are transformed at 100-120° into derivatives of 3-phenyl-2,4-dioxotetrahydroquinazoline, whereas the synthesis reported was conducted at above 200°; under these conditions the presence of a noticeable amount of (IX) can scarcely be expected.

An indirect proof of the correctness of scheme (C) is the formation of salts of aryl-N-carbamic acids during the process of the above reported transformation. Thus, after heating potassium anthranilate in a sealed tube to 220-230°, potassium phenyl-N-carbamate was found. p-Toluidine, when treated in a sealed tube with calcium anthranilate, gives rise to 4,4'-dimethylphenylurea. The obtaining of the latter is difficult to explain without assuming that the formation of p-tolyl-N-carbamic acid occurred initially.

Salts of aryl-N-carbamic acid were also found during the process of preparing aminocarboxylic acids by heating N-acylarylamines under carbon dioxide pressure. If the given process is conducted at temperatures somewhat lower than necessary for the formation of aminocarboxylic acids, then the yield of salts of aryl-N-carbamic acids attains a value of 80% of theory in a series of cases. It must be mentioned that potassium salts of aryl-N-carbamic acids are obtained by heating N-acylarylamines with K_2CO_3 under conditions of normal pressure.

Potassium salts of acyl N-carbamic acids form aminocarboxylic acids above 180° when the corresponding CO_2 pressure is used, when proceeding in open vessels at temperatures abouve 200°, they decompose with the evolution of CO_2, amine, and evidently, the di-potassium salt of aryl-N-carbamic acids.

It is completely apparent that, in the synthesis of aminocarboxylic acids from N-acylarylamines, salts of aryl-N-carbamic acids are not side products, but intermediates, whose interaction with CO_2 results in the aminocarboxylic acids.

EXPERIMENTAL

Experiments under pressure were conducted in a steel 400 ml autoclave equipped with an anchor stirrer, a socket for a thermometer, a monometer, needle valve for releasing pressure, and tube for the introduction of CO_2.

Example of the Preparation of 3-Phenyl-2,4-dioxotetrahydroquinazoline (I) and Aminobenzoic Acids. 106 g of symm-diphenylurea and 140 g of K_2CO_3 were heated under CO_2 pressure (50-55 atm) for 5 hours at 250-255°. The reaction products were mixed with 350 ml of water, and the insoluble part filtered. 10.5-11 g of p-aminobenzoic acid with traces of anthranilic acid were obtained by acidifying the filtrate to pH 6-6.5. By recrystallization from water, 7.7-7.8 g of p-aminobenzoic acid with m.p. 184-185° was obtained. The water-insoluble product, which was impure (I), was heated for 3 hours with 10% KOH, filtered, and acidified to pH 5.5-6; 6.5-7 g of anthranilic acid with m.p. 144-145° was obtained. A mixed sample with pure anthranilic acid melted at 144-145°. 6-7 g of the copper anthranilate was precipitated from filtrates with copper sulfate, which was treated with 20 ml of 2-3% sodium hydroxide, filtered, and an additional amount of anthranilic acid with m.p. 144.5-145° was isolated.

In order to obtaine pure (I), the impure product was treated with dilute hydrochloric acid, filtered, and the residue washed with water until neutral. 10.5 g of a substance with m.p. 273-274° was obtained; platelets with m.p. 276-277° (275-277° [4]) from glacial acetic acid.

3.842 mg substance: 9.970 mg CO_2; 1.424 mg H_2O. 3.132 mg substance: 8.149 mg CO_2; 1.206 mg H_2O. 3.666 mg substance: 0.390 ml N_2 (729 mm, 23.8°). 2.764 mg substance: 0.290 ml N_2 (739 mm, 18.0°). Found %: C 70.82, 71.00; H 4.15, 4.31; N 11.72, 11.96. $C_{14}H_{10}O_2N_2$. Calculated %: C 70.69; H 4.20; N.11.76.

The product is soluble in strong alkali with blue fluorescence, and upon heating of its alkaline solutions splits into anthranilic acid and aniline.

3-(3'-Methylphenyl)-2,4-dioxo-7-methyltetrahydroquinazoline. (II) and 2-Amino-4-methylbenzoic acid. 150 g of 3,3'-dimethyldiphenylurea and 100 g of K_2CO_3 were heated for 6 hours under CO_2 pressure (38-40 atm) at 220-230°. The reaction products were mixed with 250 ml of water, left to settle, and the oily layer separated. The latter was shaken for 10 minutes with 200 ml of 4% KOH (35-40°). left to settle, and the brown aqueous layer separated. 20 g of (II) precipitated on acidification. Platelets with m.p. 294-295 from glacial acetic acid.

6.204 mg substance: 16.416 mg CO_2; 3.080 mg H_2O. 5.942 mg substance: 15.728 mg CO_2; 2.824 mg H_2O. 3.990 mg substance: 0.380 ml N_2 (729 mm, 23.4°). 2.909 mg substance: 0.239 ml N_2 (743.7 mm, 20°). Found %: C 72.20, 72.23; H 5.55, 5.38; N 10.51, 10.34. $C_{16}H_{14}O_2N_2$. Caclculated %: C 72.14; H 5.26; N 10.52.

1.5 g of the product was heated for 3 hours with 70 ml of 10% KOH. On cooling, it was filtered from a small precipitate. The filtrate was extracted several times with ether. The aqueous residue of the extraction was adjusted to pH 6-6.5 with hydrochloric acid. About 0.45 g of 2-amino-4-methylbenzoic acid with m.p. 175-177° deposited; platelets with m.p. 176-177° (157° [5]) from aqueous alcohol. A mixed sample with pure 2-amino-4-methylbenzoic acid melted at 176-177°.

3-(4'-Methylphenyl)-2,4-dioxo-6-methyltetrahydroquinazoline (III) and 6-amino-3-methylbenzoic acid.

100 g of acet-p-toluidine and 100 g of K_2CO_3 were heated for 8 hours at 255-260° under CO_2 pressure. The reaction products were boiled for 3 hours with 300 ml of 5% KOH. They were filtered and 11-11.5 g of 6-amino-3-methyl benzoic acid was precipitated by acidification; platelets with m.p. 172-173° (172.5 [6]) from 50% alcohol.

3,004 mg substance: 6.970 mg CO_2; 1.608 mg H_2O. 3.904 mg substance: 9.084 mg CO_2; 2.170 mg H_2O. 4.945 mg substance: 0.419 ml N_2 (728 mm, 21°). 3.319 mg substance: 0.280 ml N_2 (727 mm, 22°). Found %: C 63.32, 63.64; H 5.99, 6.22; N 9.42, 9.33. $C_8H_9O_2N$. Calculated %: C 63.6; H 5.96; N 9.3.

By diazotization and boiling of the hydrochloric acid solution, 6-hydroxy-3-methylbenzoic acid with m.p. 149-150° (149-150° [7]) was obtained.

If the reaction mixture was acidified with hydrochloric acid after autoclaving, to a strong acid reaction to Congo, about 5 g of 3-(4'-methylphenyl)-2,4-dioxo-6-methyltetrahydroquinazoline (III) was obtained; crystals with m.p. 285-286° from 80% acetic acid.

3.312 mg substance: 8.767 mg CO_2; 1.492 mg H_2O. 3.702 mg substance: 9.784 mg CO_2; 1.736 mg H_2O. 5.862 mg substance: 0.528 ml N_2 (744 mm, 24°). 3.357 mg substance: 0.310 ml N_2 (744 mm, 23°). Found %: C 72.19, 72.08; H 5.04, 5.25; N 10.14, 10.42 M 283. $C_{16}H_{14}O_2N_2$. Calculated %: C 72.14; H 5.26; N 10.52; M 266.

The product was soluble in alkali with a blue fluorescence; it was cleaved to 6-amino-3-methylbenzoic acid, p-toluidine, and small amounts of the alkali-insoluble p-toluidide of 6-amino-3-methylbenzoic acid by a 2-hour boiling with 10% KOH. The last product was recrystallized from dilute acetic acid and melted at 182°; it gave an orange color upon the addition of a hydrochloric acid solution of nitrite to it; upon boiling in hydrochloric acid, it was cleaved to p-toluidine and 6-amino-3-methylbenzoic acid.

4.738 mg substance: 0.483 ml N_2 (746.3 mm, 21.4°). 2.685 mg substance: 0.290 ml N_2 (741 mm, 23°). Found %: N 11.87, 11.82. $C_{15}H_{16}ON_2$. Calculated %: N 11.66.

3-(3'-Chlorophenyl)-2,4-dioxo-7-chlorotetrahydroquinazoline (IV).

140 g of 3,3'-dichlorodiphenylurea and 90 g of K_2CO_3 were heated for 14 hours under CO_2 pressure (49-50 atm) to 240-245°. The oily reaction product was shaken with 400 ml of water, and the lower oily layer was separated from the water in a separatory funnel. 3 g of (IV) was isolated by treatment with dilute hydrochloric acid; platelets with m.p. 311-312° from a mixture of acetic acid and alcohol. Pure 3-(3'-chlorophenyl)-2,4-dioxo-7-chlorotetrahydroquinazoline melted at 312°. A mixed sample melted at 311-312°. The product was soluble in dilute alkali with a blue fluorescence.

(IV) was heated for 2 hours with a 10% NaOH solution, filtered, and the alkaline filtrate was extracted with ether. The aqueous residue from the extraction was acidified with hydrochloric acid to a pH of 6.5-7, and extracted with ether. Upon removal of the ether a residue of 4-chloroanthranilic acid was obtained; platelets with m.p. 234-235° (235-236° [8]) from 50% alcohol. A mixed sample with pure 4-chloroanthranilic acid melted at 234-235°.

3-(1-Naphthyl)-2,4-dioxo-7,8-benzotetrahydroquinazoline (V). Naphthylamine carboxylic acid. 92.5 g of acet-1-naphthylamine and 138 g of K_2CO_3 were heated under CO_2 pressure (20-25 atm) for 6 hours at 185-195°. The reaction mass was mixed with 350 ml of water and filtered. About 1.4 g of 1,4-naphthylaminocarboxylic acid was isolated by the neutralization of the filtrate; crystals with m.p. 177° (177° [9]) from dilute alcohol.

3.160 mg substance: 8.176 mg CO_2; 1.347 mg H_2O. 2.944 mg substance: 7.609 mg CO_2; 1.304 mg H_2O. 3.727 mg substance: 0.254 ml N_2 (741 mm, 25.5°). 3.681 mg substance: 0.242 ml N_2 (742.7 mm, 24°). Found %: C 70.57, 70.49; H 4.70, 4.96; N 7.59, 7.39. $C_{11}H_9O_2N$. Calculated %: C 70.59; H 4.81; N 7.48.

1,4-Hydroxynaphthoic acid with m.p. 179° (183-184° [10]) was obtained by diazotizing and boiling of the hydrochloric acid solution.

The water-insoluble product was boiled for 10 hours with 400 ml of 5% NaOH, filtered, and acidified. About 8 g of naphthylamine-2-carboxylic acid precipitated; platelets with m.p. 203-205° (205° [11]) from 30% alcohol.

3.440 mg substance: 8.858 mg CO_2; 1.490 mg H_2O. 3.120 mg substance: 8.017 mg CO_2; 1.342 mg H_2O. 3.673 mg substance: 0.251 ml N_2 (728 mm, 23.6°). 4.282 mg substance: 0.291 ml N_2 (735 mm, 21.4°). Found %: C 70.27, 70.12; H 4.85, 4.81; N 7.54, 7.65 $C_{11}H_9O_2N$. Calculated %: C 70.59; H 4.81; N 7.48.

1-Hydroxy-2-naphthoic acid with m.p. 184-185° (185-186° [12] was obtained by diazotization and boiling of the hydrochloric acid solution.

A dye was obtained by coupling of the diazo compound with 2-naphthol, which in contrast to dyes prepared from diazo-1,4-naphthylamine carboxylic acid, was insoluble in dilute alkalies.

To isolate (V), the reaction mixture, after autoclaving, was mixed with 5% NaOH, and filtered; the product precipitates after acidification of the filtrate. It was mixed with 100 ml of concentrated ammonia, filtered, and washed with water to neutrality. About 5 g of (V) was obtained; needles with m.p. 333-334° from glacial acetic acid.

3.302 mg substance: 9.453 mg CO_2; 1.250 mg H_2O. 3.716 mg substance: 10.643 mg CO_2; 1.432 mg H_2O. 3.750 mg substance: 0.273 ml N_2 (733.3 mm, 22°). 3.034 mg substance: 0.225 ml N_2 (732.6 mm, 22.6°). Found %: C 78.12, 78.16; H 4.24, 4.31; N 8.12, 8.26. $C_{22}H_{14}O_2N_2$. Calculated %. C 78.11; H 4.14; N 8.28.

The product was soluble in dilute alkalies; it was cleaved to 1-naphthylamine and naphthylamine-2-carboxylic acid by boiling with alkali.

Experiments on the mutual heating of potassium anthranilate and various arylamines. 120 g of potassium anthranilate and 170 g of m-chloroaniline was heated for 6 hours at 220-230° under CO_2 pressure (30 atm). The reaction mass was acidified to Congo with dilute hydrochloric acid.* 6 g of 3-(3'-chlorophenyl)-2,4-dioxotetrahydroquinazoline (VIII) was obtained; narrow interwoven platelets with m.p. 260.5-261.5° from 50% acetic acid. The product contained a small amount of 3-phenyl-2,4-dioxotetrahydroquinazoline (I), from which it could not be separated by many recrystallizations.

5.590 mg substance: 12.802 mg CO_2; 1.862 mg H_2O. 5.806 mg substance: 13.299 mg CO_2; 1.926 mg H_2O. 4.159 mg substance: 0.397 ml N_2 (734 mm, 28°). 3.641 mg substance: 0.346 ml N_2 (737.35 mm, 28°). Found %: C 62.48, 62.46; H 3.73, 3.76; N 10.44, 10.47; Cl 11.98. $C_{14}H_9O_2N_2Cl$. Calculated %: C 61.65; H 3.36; N 10.27; Cl 13.03.

The structure of the product was proved by its cleavage to anthranilic acid and m-chloroaniline by boiling with sodium hydroxide solution.

0.4 g of the substance was heated for 2 hours with 10 ml of 10% NaOH. The m-chloroaniline formed was extracted with ether; anthranilic acid with m.p. 144-145° was precipitated in the aqueous residue by adjustment to pH 6-6.5. A mixed sample with anthranilic acid melted at 145°.

m-Chloroaniline was identified by converting it to an azo dye, for which the ether extract was treated with dilute hydrochloric acid, diazotized, and the diazo compound coupled with 2-naphthol. A dye was obtained (scale-like platelets from glacial acetic acid) with m.p. 155-156°. The crystals from pure m-chloroaniline and 2-naphthol melted at 155-157°. A mixed sample melted at 155-157°.

100 g of potassium anthranilate and 150 g of m-toluidine were heated for 5 hours at 225-230° under CO_2 pressure (26-28 atm.). The reaction mixture was acidified to Congo with dilute hydrochloric acid. The precipitate which separated was mixed with 200 ml of 5% NaOH and filtered. About 7.5 g of the product with m.p. 225-230° was isolated from the filtrate by acidifying to Congo. Two recrystallizations from 50% acetic acid with activated carbon resulted in spindlelike crystals of 3-(3'-methylphenyl)-2,4-dioxotetrahydroquinazoline (VI) with m.p. 252-252.6°.

5.356 mg substance: 14.018 mg CO_2; 2.276 mg H_2O. 5.562 mg substance: 14.510 mg CO_2; 2.304 mg H_2O. 0.1950 g substance: 15.64 ml 0.1N HCl. 0.2154 g substance: 17.17 ml 0.1 N HCl. Found % C 71.40; 71.42; H 4.75, 4.64; N 11.23, 11.16. $C_{15}H_{12}O_2N_2$. Calculated %: C 71.43; H 4.76; N 11.11.

0.6 g of the substance was boiled for 4 hours with 15 ml of 10% KOH, diluted with water, and about 0.1 g of a silvery precipitate, the m-toluidide of anthranilic acid, m.p. 113-114° (113-114° [13]) was filtered. A mixed sample with pure anthranilic acid m-toluidide melted at 113-114°. m-Toluidine was extracted with ether from the the filtrate, and anthranilic acid with m.p. 144-145° was isolated upon adjustment to pH 6-6.5. A mixed sample with pure anthranilic acid melted at 144-145°.

100 g of potassium anthranilate and 150 g of p-toluidine were heated for 7 hours at 230-235° under CO_2 pressure (27-30 atm). A precipitate formed by acidifying the reaction products with dilute hydrochloric acid, which was treated with 5% NaOH solution. A small precipitate was filtered; thin needles of 4,4'-dimethyldiphenylurea with m.p. 262° (262-263° [14]) were obtained by recrystallization first from acetic acid, and then from alcohol. A mixed sample with pure 4,4'-dimethyldiphenylurea melted at 262.5°.

12.2 g of a substance with m.p. 240-245° was isolated from the alkaline filtrate by acidifying to Congo; needles of 3-(4'-methylphenyl)-2,4-dioxotetrahydroquinazoline (VII) were obtained from glacial acetic acid, which melted at 249-250° initially, then solidified, and once more melted at 259-260° (259-260° [15]).

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* The insoluble product was filtered out and washed with water to neutrality.

6.080 mg substance: 15.882 mg CO_2; 2.610 mg H_2O. 6.548 mg substance: 17.107 mg CO_2; 2.922 mg H_2O. 3.250 mg subs.: 0.303 ml N_2 (733.2 mm, 19°). 4.276 mg substance: 0.407 ml N_2 (732.4 mm, 20°). Found %: C 71.28, 71.30; H 4.80, 4.99; N 10.51, 10.69. $C_{15}H_{12}O_2N_2$. Calculated %: C 71.43; H 4.76; N 11.11.

1 g of the product was refluxed in a flask for 6 hours with 25 ml of 10% KOH. As the heating progressed, the solution clouded and p-toluidine droplets (m.p. 44°) formed in the condenser. At the end of this time, it was filtered. There was about 0.15 g of anthranilic acid p-toluidide, m.p. 149-150° (151° [16]) in the residue. Anthranilic acid, m.p. 144-145°, was liberated by acidification of the alkaline filtrate. A mixed sample with pure anthranilic acid melted at 144-145°.

15 g of potassium anthranilate was heated for 8 hours at 230-240° in a 175 ml sealed glass tube. A pressure was detected upon opening the tube at the end of the experiment. The reaction products were treated with hydrochloric acid. 1 g of 3-phenyl-2,4-dioxotetrahydroquinazoline (I) melting at 276-277° was obtained. A mixed melting point with (I) obtained by heating diphenylurea with K_2CO_3 under CO_2 pressure gave no depression.

10 g of potassium 2-amino-4-methylbenzoate was heated for 8 hours in a sealed tube at 220-230°. Pressure was observed upon opening the tube. The reaction products were processed in the previous manner. About 0.6 g of 3-(4'-methylphenyl)-2,4-dioxotetrahydroquinazoline (III) was obtained; crystals with m.p. 285-286° from acetic acid. A mixed sample with (III) obtained by heating acet-p-toluidide with K_2CO_3 under CO_2 pressure melted at 285-286°.

Potassium aryl-N-carbamates. 106 g of diphenylurea and 138 g of K_2CO_3 were heated in the autoclave for 8 hours at 175-180° under CO_2 pressure (30-40 atm). A white powder was obtained, which was the potassium salt of phenyl-N-carbamic acid with impurities of K_2CO_3 and a small amount of unreacted diphenylurea. The yield of potassium N-phenylcarbamate was about 80% of theory. The product was treated with pyridine, filtered, and washed with ether to remove the impurity of diphenylurea.

15 g of the substance purified in this manner was heated to 40° with 45 ml of pyridine, 20 ml of methyl benzenesulfonate was added over a 3 hour period, the reaction mass was kept for 1 hour at 50°, cooled, filtered, the filtrate evaporated in vacuum (15 mm) on the boiling water bath, acidified to Congo with hydrochloric acid, and extracted with ether. Methyl phenyl-N-carbamate remained after the removal of the ether; needles with m.p. 47° (47° [17]) from 50% alcohol. A mixed sample with pure methyl phenyl-N-carbamate melted at 47°.

3.394 mg substance: 7.970 mg CO_2; 1.870 mg H_2O. 3.680 mg substance: 8.643 mg CO_2; 1.950 mg H_2O. 3.650 mg substance: 0.283 ml N_2 (749.2 mm, 21°). 3.922 mg substance: 0.299 ml N_2 (748.8 mm, 21°). Found %; C 64.08, 64.10; H 6.17, 5.93; N 8.88, 8.72. $C_8H_9O_2N_2$. Calculated %: C 63.57; H 5.96; N 9.27.

15 g of 3,3'-dichlorodiphenylurea, 11 g of K_2CO_3, and 30 ml of m-chloroaniline were heated for 10 hours at 185-190° with efficient stirring in a flask equipped with a straight condenser in a slow stream of CO_2. The residue was freed from the residual 3,3'-dichlorodiphenylurea by treatment with pyridine, filtration, and washing with ether. Potassium-3-chlorophenyl-N-carbamate contaminated with K_2CO_3 was obtained. Yield about 50% of theoretical. The product was soluble in alkalies. Upon standing in alkaline solution, hydrolysis occurred with formation of 3-chloroaniline.

SUMMARY

1. On heating N-acylarylamines with K_2CO_3 under CO_2 pressure, aminocarboxylic acids, derivatives of 3-phenyl-2,4-dioxotetrahydroquinazoline, and salts of aryl-N-carbamic acids were formed; the latter were also obtained upon heating a series of N-acylarylamines in the absence of CO_2 under normal pressure.

2. 3-Phenyl-2,4-dioxotetrahydroquinazoline and its derivatives were formed by heating potassium salts of aromatic o-aminocarboxylic acid; on heating potassium anthranilate with a series of arylamines, derivatives of 3-phenyl-2,4-dioxotetrahydroquinazoline were formed.

3. In view of the fact that, during the process of heating N-acylarylamines with K_2CO_3 under CO_2 pressure, some of them are transformed, to an 80-85% extent, to the potassium salt of aryl-N-carbamic acid before the start of the formation of aminocarboxylic acids, as well as the fact that heating potassium salts of phenyl-N-carbamic acids leads to the formation of aminocarboxylic acids, it is quite apparent that salts of aryl-N-carbamic acids are not side, but intermediate, reaction products, which are the source of the formation of ions of arylamines which react with CO_2 and form amino acids.

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INVESTIGATION OF CONJUGATED SYSTEMS

XLVII. CONDENSATION OF BUTYNONE WITH CYCLIC DIENIC HYDROCARBONS

A. A. Petrov and N. P. Sopov

Of the large number of papers on "dienic syntheses", an insignificant number is about investigations on the condensation of dienic compounds with acetylenic aldehydes, ketones, acids, and derivatives of acids [1]. Only several condensations of dienic compounds with acetylene dicarboxylic and phenylpropiolic acids and their derivatives have been reported, as well as those in which propiolic, tetrolic, and phenylpropiolic aldehydes participated [2-4]. The authors of this communication studied the reactions of the simplest acetylenic ketone, butynone, with divinyl, isoprene, piperylene, dipropenyl, diisopropenyl, and chloroprene [5-7]. Several dienic syntheses with the participation of butynone, and other acetylenic ketones (propylacetylenyl ketone, phenylacetylenyl ketone, propenylacetylenylketone, dibenzoylacetylene) were reported by foreign chemists [8, 9]. Recently an unusual condensation of butynone with methylcyclohexanones by another scheme was reported.

Continuing the investigation of the reactions of butynone with dienic compounds, experiments were conducted on the condensation of this substance with cyclic dienic hydrocarbons, cyclopentadiene-1,3 and cyclohexadiene-1,3.

Previously the condensation of these hydrocarbons with acetylenic compounds was studied only with vinylacetylenyl ketone, acetylene dicarboxylic acid, its esters, and nitrile [11-17].

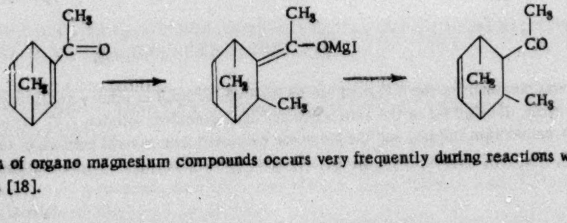
Cyclopentadiene, with all of these compounds, gives even at room temperature, comparatively stable condensation products with endo-methylene bridges, which decompose into the starting components upon heating [11-14].

Cyclohexadiene at 0° gives a normal condensation product with acetylene dicarboxylic acid, a dibasic acid with an endo-ethylene bridge. However, this product readily loses an ethylene molecule on heating and gives phthalic acid [15]. The condensation of cyclohexadiene with acetylene dicarboxylic acid esters at 200° gives phthalic acid esters directly [16].

The experiments conducted showed that cyclopentadiene readily condenses with butynone even at 50° with the formation of two products as a result of the reaction, a liquid and a crystalline substance.

The liquid product was found to be the normal condensation product of cyclopentadiene and butynone, 1-acetyl-3,6-endomethylene-cyclohexadiene-1,4, which readily formed a semicarbazone.

Attempts to obtain tertiary alcohols from this ketone by the action of methyl magnesium iodide and bromide under conditions previously used for the synthesis of tertiary alcohols from cyclohexadienic ketones [17] ended unsuccessfully. A ketone with another methyl group was obtained instead of the alcohol. Evidently, the organo magnesium compound added to the starting ketone at the conjugated system of bonds according to the scheme:

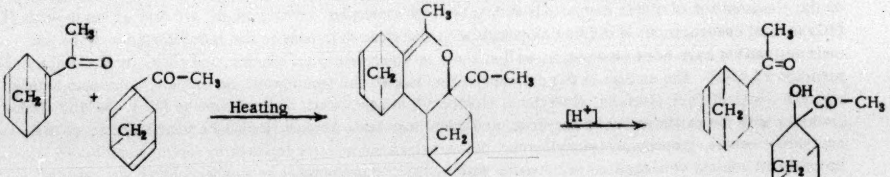


Such an addition of organo magnesium compounds occurs very frequently during reactions with α,β-unsaturated ketones [18].

The ketone obtained, 1-methyl-2-acetyl-3,6-endomethylenecyclohexene-4, readily formed a well crystallizing semicarbazone and 2,4-dinitrophenylhydrazone.

The crystalline condensation product with m.p. 107° was found to be the dimer of the liquid ketone. It was readily obtained from the latter by heating, as well as by prolonged storage. Each redistillation of the liquid ketone (at 10mm) was accompanied by the formation of small amounts of this crystalline dimer in the distillation flask. The dimer distills at 183-185° without apparent decomposition at 10 mm. The substance has the same empirical formula as the liquid ketone but a double molecular weight, it gives a positive result upon testing for the presence of a carbonyl group (reaction with p-nitrophenylhydrazine), and does not contain hydroxyl groups (determined according to Teretyev).

Acetylendomethylencyclohexadiene can form a dimer analogous to that of methylacrolein [19] resembling the reaction of acrolein with vinyl ethers [20], namely according to the scheme:

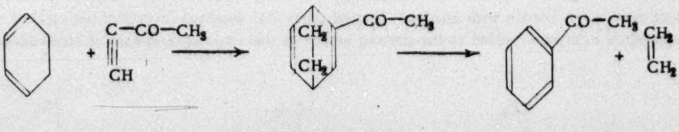


The proposed formula for the dimer was proved by its relation to acids. It readily rearranged by the action of acids to a substance with a higher melting point containing two carbonyl groups (it gives a double p-nitrophenylhydrazine) and a hydroxyl group (determined according to Terentyev, giving a result two times the theoretical amount evidently because the organo magnesium compound causes the dehydration of the substance).

The formation of the dimer from the condensation products of cyclopentadiene with α,β-unsaturated carbonyl compound had not been found up to the present investigation.

Cyclohexadiene practically does not condense with butynone at 50°. At 90°, the reaction proceeds slowly, forming acetophenone and ethylene as the main products In addition to acetophenone, a very small amount of a higher boiling substance was formed, which, however, was not isolated in pure state. Apparently, this is the normal product of the condensation with an endo-ethylene bridge. At 120°, the reaction proceeds with the formation of acetophenone and ethylene exclusively. Acetophenone was identified by constants and melting point of its 2,4-dinitrophenylhydrazone. Ethylene was absorbed by bromine and identified as dibromoethane.

Therefore, the condensation of butynone and cyclohexadiene is accompanied by the cleavage of the endo-ethylene bridge by the scheme:



EXPERIMENTAL

Butynone was obtained for the investigation by shaking methoxy or ethoxyvinylacetylene with 5g H_2SO_4 (for 8-10 g of the ether, 100-120 ml of the acid was used) until complete solution [21]. The solution obtained was saturated with ammonium sulfate, and the butynone extracted with several portions of toluene. The subsequent experiments were conducted with these solutions dried with anhydrous soldium sulfate.

Cyclopentadiene was obtained by the slow distillation of the dimer; cyclohexadiene, by the distillation of 1,2-dibromocyclohexane with quinoline. Cyclohexadiene contained cyclohexene as an impurity which did not interfere in the subsequent experiments since cyclohexene does not condense with butynone under the usual conditions of the dienic synthesis.

1. Condensation of cyclopentadiene with butynone.

In one of these experiments 13.5 g (17 ml) of cyclopentadiene was heated in a sealed glass tube for 6 hours at 90° with a solution of butynone in toluene prepared from 16 g of ethoxyvinylacetylene. By vacuum distillation (toluene was removed at 50 mm and the residue was distilled at 10 mm), 12 g of a liquid product (90-95°) and 5 g of residue were obtained which boiled at 183-185° and crystallized upon standing.

The liquid reaction product came over mainly at 92° (20 mm) upon redistillation and had

d_4^{20} 1.0362, n_D^{20} 1.5098. MR_D found: 38.71. $C_9H_{10}O$. Calculated: 38.44.

0.1312 g substance: 0.3862 g CO_2; 0.0894 g H_2O. Found %: C 80.33; H 7.62. $C_9H_{10}O$. Calculated %: C 80.56; H 7.51.

The substance polymerized partly upon redistillation, and upon standing, with the formation of a crystalline product (identical with that isolated directly from the reaction mixture) and tars. A semicarbazone with m.p. 166-167° was obtained from the substance. It could not be recrystallized. A ketone (4.3 g) with b.p. 94.5-95° at 20 mm was obtained in 55% yield by the reaction of 7 g of the substance with two equivalents of an ether solution of methyl magnesium iodide under the usual conditions;

d_4^{20} 0.9905, n_D^{20} 1.4846. Found MR_D 43.44. $C_{10}H_{14}O$. Calculated 43.52.

8.59 mg substance: 25.33 mg CO_2; 7.28 mg H_2O. Found %: C 80.47; H 9.47. $C_{10}H_{14}O$. Calculated %: C 79.95; H 9.40.

A semicarbazone and 2,4-dinitrophenylhydrazone were obtained from the ketone under the usual conditions. The semicarbazone was recrystallized from aqueous alcohol. M.p. 178°.

9.78 mg substance: 1.616 ml N_2 (16°, 770 mm). Found %: N 19.78. $C_{11}H_{17}ON_3$. Calculated %: N 20.27.

The 2,4-dinitrophenylhydrazone had an m.p. 182.5-183.5° (it was recrystallized from dilute alcohol).

3 g of the ketone was distilled with a 10% solution of oxalic acid; the substance distilled unchanged. Therefore, it was shown that it did not contain any tertiary alcohol as an impurity.

The same ketone with b.p. 92-94° at 20 mm was obtained by the action of a double quantity of an ether solution of methyl magnesium bromide upon acetylendomethylenecyclohexadiene; d_4^{20} 0.9886, n_D^{20} 1.4886.

The crystalline product of the condensation of cyclopentadiene with butynone was washed with several portions of cold methanol; it then weighed 3.5 g. After recrystallization from methyl alcohol the substance melted at 107° and was a white dense crystalline substance.

0.1292 g substance: 0.3788 g CO_2; 0.0880 g H_2O. 0.1308 g substance: 0.3860 g CO_2; 0.0882 g H_2O. 0.1206 g substance: 20.0 g benzene: Δt 0.115°. Found %: C 80.01, 80.53; H 7.62, 7.54; M 268.5. $C_{18}H_{20}O_2$. Calculated %: C 80.56; H 7.51; M 268.3.

The substance gave a binary p-nitrophenylhydrazone with m.p. 182-183°[*] with p-nitrophenylhydrazine in acetic acid, which corresponded in analytical data to the p-nitrophenylhydrazone of the product of hydrolysis of the starting substance.

6.88 mg substance: 0.871 ml N_2 (17°, 762.5 mm). 8.90 mg substance: 1.185 ml N_2 (18°, 749 mm). Found %: N 14.95, 15.39. $C_{30}H_{32}O_5N_6$. Calculated %: N 15.10.

Upon heating 1 g of the substance with 5 ml of acetic acid for 30 minutes and after neutralization of the mixture with sodium carbonate, about 0.9 g of product was obtained which melted at 127-128° after recrystallization from aqueous acetone.

7.20 mg substance: 19.90 mg CO_2; 5.18 mg H_2O. 9.24 mg substance: 25.48 mg CO_2; 6.45 mg H_2O. 0.1386 g substance: 16.57 g benzene: Δt 0.152°. Found %: C 75.43, 75.25; H 8.05, 7.81; M 284.4. $C_{18}H_{22}O_3$. Calculated %: C 75.49; H 7.74; M 286.3.

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[*] Without recrystallization.

The determination of the active hydrogen according to Terentyev gave twice the calculated result.

0.0376 g substance: 6.94 ml CH_4 (15°, 751 mm). 0.0440 g substance: 7.80 ml CH_4 (18°, 755 mm). Found number of active H atoms: 2.04, 2.06. $C_{18}H_{21}O_2OH$. Calculated 1.0.

The same binary p-nitrophenylhydrazone, m.p. 182-183° (without recrystallization) was obtained from the substance with m.p. 127-128° in acetic acid as was obtained from the substance with m.p. 107°, however, with a poorer yield.

6.63 g substance: 0.863 ml N_2 (18°, 750.5 mm). Found %: N 15.08. $C_{30}H_{32}O_5N_6$. Calculated %: N 15.10.

Upon heating cyclopentadiene (8 g) with butynone (from 7.8 g of ethoxyvinylacetylene) at 50° for 6 hours, 6.2 g of a liquid and about 1 g of a crystalline product was obtained.

2. Condensation of cyclohexadiene with butynone.

a) 12 g of cyclohexadiene was heated for 6 hours in a sealed tube with a toluene solution of butynone obtained from 12 g of ethoxyvinylacetylene. After distillation at reduced pressure of the toluene and the reagents, no higher boiling residue remained in the flask.

b) The same amounts of the reagents were heated for 10 hours at 100-105°. After the removal of the toluene, 4 g of a substance remained in the flask, which was separated into the following fractions upon distillation (10 mm): 1) 80-85°, 2 g; 2) 85-91°, 1 g; 3) 91-93°, 0.8 g. The last fraction had n_D^{20} 1.5212.

The first fraction was found to be acetophenone. The last fraction had constants which differed from those found for acetophenone (b.p. 83-85° at 12 mm, d_4^{25} 1.0236, n_D^{20} 1.5342) [22]. However this fraction gave a 2,4-dinitrophenylhydrazone, which was characteristic for acetophenone dinitrophenylhydrazone with m.p. 236°. Evidently, the substance is a mixture of acetophenone and the normal product of the condensation.

c) Upon heating the same quantities of the reagents at 120° for 6 hours, 6 g of acetophenone was obtained (yield 40%) with b.p. 94.5° at 20 mm d_4^{20} 1.0290, n_D^{20} 1.5344; the p-nitrophenylhydrazone of the substance melted at 184°, the 2,4-dinitrophenylhydrazone at 237°, which accurately corresponded to the literature data. A pressure was detected when the tube was opened. Several of the tubes were cooled with a mixture of ice and salt prior to opening, and the gas which was evolved after their opening, was passed into bromine. A small amount of dibromoethane with b.p. 131-133° and n_D^{20} 1.5380 was obtained. Literature data: [22], b.p. 131.7°, n_D^{20} 1.5379.

SUMMARY

1. The condensation of butynone with cyclopentadiene-1,3 and cyclohexadiene-1,3 was studied.

2. It was shown that cyclopentadiene gave a normal condensation product, 1-acetyl-3,6-endomethylenecyclohexadiene-1,4, capable of being transformed into a crystalline dimer, constructed analogously to that of methylacrolein, upon heating and upon storage.

3. It was shown that cyclohexadiene condensed with butynone with the cleavage of a molecule of ethylene to form acetophenone.

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* See Consultants Bureau Translation, p. 949.

INVESTIGATIONS OF CONJUGATED SYSTEMS

XLVIII. ORDER OF ADDITION OF ALKYL HYPOIODITES TO CHLOROPRENE HOMOLOGS

A. A. Petrov and E. A. Leporskaya

Investigation of reactions of chloroprene and bromoprene with alkyl hypohalites conducted by one of the authors led to unexpected results. It was found that the order of addition depends on the nature of the halogen. Alkyl hypochlorites added to chloroprene and bromoprene mainly at the ends of the conjugated system [1,2], i.e., in a similar manner as halogens [3,4,5] and hydrogen halides [6,7,8] add to these substances, with the chlorine entering position one. Alkyl hypobromites and hypoiodites added almost exclusively to the unsubstituted double bond with the halogen atoms entering position 4 [9,10,11]. Therefore, only alkyl hypochlorites were found able to polarize the entire dienic system as a whole.

This eccentricity in the reactions of chloroprene and bromoprene with alkyl hypohalites was explained by steric and energetics factors. Chlorine or bromine atoms in position 2 of the chloroprene and bromoprene molecules, possibly, interfere with the entrance of bromine and iodine atoms into position 1, whereas this barrier is insufficient for the entrance of chlorine. It is possible that here the great heat of reaction of alkyl hypochlorites with dienes is of effect because of which a more complete polarization of the systems exists in the reaction complex.

The necessity to establish the mechanism of this effect caused the authors to investigate the order of addition of alkyl hypohalites to homologs of chloroprene and bromoprene. The present communication deals with the investigation of the order of addtion of alkyl hypoiodites to homologs of chloroprene with radicals in the α-position of the conjugated system $R-CH=CCl-CH=CH_2$.

α-Alkyl derivatives of chloroprenes were first prepared by the addition of hydrogen chlorides to α-alkyl derivatives of vinylactylene [12]. The latter was prepared by the action of alkylating agents on sodium derivatives of vinyl acetylene in liquid ammonia [13]. This method was used.

The chemical properties of the chloroprene homologs were scarcely studied. Authors who first obtained these compounds only investigated their condensation with naphthoquinone and polymerizations. Up to now, no one had studied these compounds.

5 substances were prepared for the investigation, whose formulas and constants are given in Table 1. Two substances were previously unsynthesized.

TABLE 1

Substance	B.p. (° C)	Pressure (mm)	d_4^{20}	n_D^{20}	MR_D		Literature
					Found	Calculated	
$CH_2=CH-CCl=CH-CH_3$	100	760	0.9592	1.4782	30.72	29.22	–
	99.5-101.5	759	0.9576	1.4785	30.33	29.22	[13]
$CH_2=CH-CCl=CH-C_2H_5$	122.5-123.5	760	0,9392	1.4772	35.09	33.84	–
	68.2-69	117	0.9390	1.4770	35.08	33.84	[13]
$CH_2=CH-CCl=CH-C_3H_7$	49.5-50.5	20	0.9290	1.4798	39.93	38.46	–
$CH_2=CH-CCl=CH-C_4H_9$	69.5-70.5	20	0.9185	1,4782	44.58	43.08	–
	64-65	18	0.9366	1.4794	43.82	43.08	[13]
$CH_2=CH-CCl=CH-(CH_2)_2-$ $-CH(CH_3)_2$	83.5-84.5	20	0.9134	1.4770	49.08	47.70	–

TABLE 6

Substance	Weight of sample (g)	Weight AgCl (g)	%Cl	
			Found	Calculated
$CH_2{=}CH{-}CCl{=}CH{-}C_3H_7$	0.1301	0.1424	27.08	27.15
	0.1246	0.1380	27.42	27.15
$CH_2{=}CH{-}CCl{=}CH{-}(CH_2)_2{-}CH(CH_3)_2$	0.1340	0.1193	22.02	22.34

Isopropylvinylacetylene and tertiarybutylvinylacetylene could not be obtained; in both cases, hydrogen halide was cleaved from the halogen derivative to form propylene and isobutylene, respectively.

In addition to isobutylene, a hydrocarbon derived from isobutyl bromide was obtained in very low yields. Further experiments were not conducted with these substances Propylene and butylene were identified as dibromides: the gas which separated, after the absorption of ammonia with water and dilute acid, was passed into a bromine solution.

Dibromopropane had the following constants b. p. 141-142°; d_4^{20} 1.9344; n_D^{20} 1.5202. Literature data: b.p. 141.6°; d_4^{20} 1.9333.

Dibromomethylpropane had the following constants: b. p. 150-151°; d_4^{20} 1.7676; n_D^{20} 1.5100. Literature data [15]: b.p. 149-151°; d_4^{20} 1.7827; n_D^{20} 1.5119.

II. Preparation of Chloroprene Homologs

1 Mole of the hydrocarbon, 220 ml of hydrochloric acid, saturated with hydrogen chloride, at 0°, 0.25 mole of $CuCl_2$, and 0.2 moles of methylamine hydrochloride, or ammonium chloride (0.2 g of hydroquinone) were shaken for 9 hours, the water layer was separated, the oil washed with water, dried over $CaCl_2$, and fractionated through a dephlegmator.

The yields of the chloroprenes boiling within 1-2° were: 3-chloropentadiene-1,3 (36%), 3-chlorohexadiene-1,3 (27%) 3-chloroheptadiene(36%), 2-chlorooctadiene and 3-chloro-7-methyloctadiene-1,3 (15%), based on the hydrocarbon used. The unreacted hydrocarbons were once more hydrochlorinated. The total yield for two consecutive hydrochlorinations was 27% for chlorooctadiene and chloromethyloctadiene. Table 6 gives the analytical results for the new compounds prepared.

III. Iodoalkoxylation of Chloroprene Homologs

1. Iodomethoxylation of 3-chloropentadiene-1,3. 48 g of mercuric oxide was added to a solution of 29.5 g chloropentadiene (0.2 g hydroquinone) in 80 ml of methyl alcohol, and 74 g of powdered iodine was added slowly with efficient stirring and cooling (temperature of the reaction mixture, 10-12°) in 5 g portions. After the addition of each portion of iodine, the mixture was shaken and stirred until decolorization. At the end of the reaction, the unreacted mercuric oxide and the mercuric iodide were filtered and washed with alcohol on the filter, the filtrate was diluted with water, the oil which separated was washed with calcium chloride solution to remove the alcohol, dried over $CaCl_2$ and vacuum distilled The fractions were obtained (5 mm): 1) 70-80°- 6 g, 2) 82-83°-39 g and 3) residue, 3.5 g. Yield of the main fraction, 52% of theory. The constants of the substance are in Table 2, the analytical data in Table 7.

2. Iodomethoxylation of 3- chlorohexadiene-1,3. An oil was obtained under the above conditions from 24 g of chlorohexadiene, 60 ml of methyl alcchol, 33.5 g of mercuric oxide, and 52.6 g of iodine, which gave the following fractions upon distillation (at 10 mm): 1) 80-90°-1.9 g, 2) 90-100°- 1.6 g, 3) 100-104°-3.5 g 4) 104-106° - 17g, 5) 106-110°, 3.1 g, 6) residue, 4.2 g. Yield of the main (100-110°) fraction, 42.7% of theory. Constants are given in Table 2, analytical data in Table 7.

About 4 g of propionic and 4 g of oxalic acids were obtained after the usual processing of the mixture, by the oxidation of 33 g of the iodoether at 10° with 760 ml of a 5% potassium permanganate solution, to which 8 g more of permanganate was added in small portions. The propionic acid was converted into an anilide with m.p. 104°; in addition a p-toluidide with m.p. 123° was also obtained from it. Neither crystalline product gave any depression in mixed melting point with authentic preparations of propionic acid anilide and p-toluidide.

3. Iodoethoxylation of chlorohexadiene, 13 g of a substance was obtained from 10 g of chlorohexadiene, 60 ml of ethyl alcohol, 14 g of mercuric oxide, and 22 g of iodine, which gave the following fractions upon distillation (10 mm): 1) up to 107°- 1.0 g, 2) 107-109°-10.4 g, 3) 109-111°- 1.5 g.

Constants of the main part of the substances are given in Table 2, analytical data, in Table 7.

4. Iodomethoxylation of chloroheptadiene. An oil was obtained from 20 g of chloroheptadiene, 60 ml of alcohol, 35 g of mercuric oxide, and 57 g of iodine, which gave the following fractions upon distillation (10 mm): 1) to 114°, 6 g; 2) 114-117°, 40 g; 3) residue, 4 g. Yield of the main fraction, 63%. The constants are given in Table 2, analytical results in Table 8.

TABLE 4

Substance	B.p. (°C)	Pressure (mm)	d_4^{20}	n_D^{20}	MR_D		Melting point		
					Found	Calculated	Semicarbazone	p-nitrophenylhydrazone	2,4-dinitrophenylhydrazone
$CH_3-CO-CCl=CH_2$	38-40	30	1.1373 (15°)	1.4608 (15°)	25.21	25.08	139-140	100-103	–
$CH_3-CO-CCl=CH-CH_3$	65-66	30	1.0966	1.4742	30.33	29.70	–	122	188
$CH_3-CO-CCl=CH-C_2H_5$	76-77.5	30	1.0592	1.4730	35.12	34.32	–	–	139
$CH_3-CO-CCl=CH-C_3H_7$	91-93	30	1.0301	1.4720	39.85	38.94	–	111.5-112	144
$CH_3-CO-CCl=CH-C_4H_9$	108-111	30	1.0070	1.4705	44.55	43.56	–	117-118	108
$CH_3-CO-CCl=CH-(CH_2)_2-CH(CH_3)_2$	118-120	30	0.9836	1.4662	49.21	48.18	168	105	131
$CH_3-CO-CClBr-CH_2Br$	83-83.5	10	2.0084	1.5375	41.15	41.15	–	–	–
$CH_3-CO-CClBr-CHBr-CH_3$	94.5-95	10	1.8689	1.5348	46.36	45.70	–	–	–

TABLE 5

Substance	B.p. (°C)	Pressure	d_4^{20}	n_D^{20}	MR_D	
					Found	Calculated
$CH_2=CH-C\equiv C-CH_3$	59-59.5	760	0.7396	1.4450	23.72	22.77
	59.2	760	0.7401	1.4496[13]	23.98	22.77
$CH_2=CH-C\equiv C-C_3H_7$	83.5-84	760	0.7479	1.4522	28.91	27.34
	84.5-85.3	–	0.7492	1.4522[13]	28.86	27.34
$CH_2=CH-C\equiv C-C_3H_7$	109.5-110	760	0.7603	1.4524	33.43	32.00
	44.3-44.7	75	0.7671	1.4520[14]	33.00	32.00
$CH_2=CH-C\equiv C-C_4H_9$	62-64	60	0.7763	1.4568	37.93	36.61
	62-63	61	0.7830	1.4592[13]	37.84	36.61
$CH_2=CH-C\equiv C-CH_2-CH(CH_3)_2$	54-56	60	0.7668	1.4440	37.48	36.61
$CH_2=CH-C\equiv C-(CH_2)_2-CH(CH_3)_2$	76-77	60	0.7803	1.4571	42.66	41.23

Therefore, the complete analogy between the reaction of chloroprene with alkyl hypoiodites and that of its homologs with alkyl hypoiodites was shown by the results of this investigation.

EXPERIMENTAL

I. Preparation of Alkylvinylacetylenes

40 g of powdered sodium amide was dissolved with efficient stirring in 1 liter of liquid ammonia over a 6-8 hr. period; gaseous vinylacetylene (100 ml of the liquid vinylacetylene, 25% excess) was then passed into the solution over a 6-8 hour period. The corresponding alkyl bromide (1 mole) was added drop wise (methyl bromide) was passed in as a gas) over 8-10 hours through a tube going to the bottom of the flask into the sodium vinylacetylide solution obtained At the end of the reaction, the mixture was allowed to stand in order to evaporate the ammonia, whereby the alkylvinylacetylene which was distilling with the ammonia was condensed in absorbers filled with water and cooled with snow. The residue in the flask was treated with the ammonia solution from the absorption bottles, the oily layer collected in the absorption apparatus was added to it, and the mixture distilled. The lighter layer collected in the receiver, cooled with ice, over the ammonia water, was separated, washed 2 times with water, and dilute HCl solution, and distilled through a dephlegmator. Constants of the 7 substances obtained are given in Table 5.

The yield of the methyl homolog was 40-45% of theory, the ethyl about 50%, the propyl 80%, butyl 80%, isoamyl 73%.

TABLE 3

Substance	B.p., °C (85 mm)	d_4^{20}	n_D^{20}	MR_D	
				Found	Calculated
$CH_2{=}C(OCH_3){-}CCl{=}CH_2$	58.5-59.5	1 0579	1.4712	31.34	30.86
$CH_2{=}C(OC_2H_5){-}CCl{=}CH_2$	74.5-75	1.0204	1.4641	35.86	35.48
$CH_2{=}C(OCH_3){-}CCl{=}CH{-}CH_3$	85-86	1.0392	1.4798	36.23	35.48
$CH_2{=}C(OCH_3){-}CCl{=}CH{-}C_2H_5$	102-103.5	1.0179	1.4792	40.86	40.10
$CH_2{=}C(OC_2H_5){-}CCl{=}CH{-}C_2H_5$	113.5-114.5	0.9875	1.4708	45.45	44.72
$CH_2{=}C(OCH_3){-}CCl{=}CH{-}C_3H_7$	119-120	0.9966	1.4790	45.71	44.72
$CH_2{=}C(OCH_3){-}CCl{=}CH{-}C_4H_9$	137.5-139.5	0.9833	1.4778	50.27	49.33
$CH_2{=}C(OCH_3){-}CCl{=}CH{-}(CH_2)_2{-}CH(CH_2)_2$	146-147	0.9684	1.4738	54.74	53.95
$CH_2{=}C(OC_2H_5){-}CCl{=}CH{-}(CH_2)_2{-}CH(CH_3)_2$	158-161	0.9656	1.4732	58.92	58.57

from chloroprene.

It is apparent from the data in Table 2 that the boiling point rises, and the density and refractive index decreases regularly in the homologous series of these ethers. All ethers have a specific odor (senna), are insoluble in water, and color upon storage as a result of the separation of iodine.

Hydrogen iodide is readily cleaved by the action of alkalies to form chloroalkoxyprene homologs The physical properties of the substances obtained are compared in Table 3 with those of the previously obtained chloroalkoxyprenes.

It is apparent from the data in Table 3, that all of the substances boiled within a 1-3° range, and evidently, are a mixture of cis and trans isomers Just as with the iodo ethers series, a regular rise in boiling point and decrease of density and refractive index occurs. All of the substances show an exaltation of about 0.5-0.9 units in the molar refractivity. The freshly prepared substances are colorless; they turn yellow and tar, and are transformed into viscous products. However, they are more stable than the chloroalkoxyprenes.

All of the ethers obtained are saponified to the corresponding ketones by dilute acids according to the equation:

$$CH_2{=}C(OR){-}CCl{=}CH{-}R \rightarrow CH_3{-}CO{-}CCl{=}CH{-}R\ .$$

The rate of saponification drops strongly in the homologous series. The ether with an isoamyl radical does not saponify completely after shaking for 10 hours with 5% H_2SO_4 at 40-50°.

The properties of the ketones obtained in this manner are given in Table 4, as well as those of the ketone obtained from chloroprene.

It is apparent from the data of Table 4 that the usual generalizations are found in the homologous series of these substances. All of the substances exhibit exaltation in the molecular refractivity.

Bromination, reduction, and formation of hydrazone were investigated from among the chemical properties of these ketones. All of the ketones readily brominate in chloroform solution with bromine; however, only the bromination product of the first ketone could be distilled. The rest of the substances decomposed upon distillation, forming hydrogen bromide. The reduction of these bromides with zinc proceeds with separation of hydrogen bromide, as a result of which a mixture of saturated and unsaturated ketones was obtained. The corresponding product from chloroprene was smoothly reduced to methyl ethyl ketone under these conditions

The reduction of unsaturated chloroketones with colloidal platinum could not be realized because of the systematic poisoning of the catalyst.

The rate of semicarbazone formation decreases sharply with the increase in the size of the radical; p-nitrophenylhydrazones are formed readily upon heating; the semicarbazones are greatly affected for this reason, their melting points are not sharp; the 2,4-dinitrophenyl hydrazones melt more sharply.

TABLE 2

Substance	B.p. (°C) (10 mm)	d_4^{20}	n_D^{20}	MR_D	
				Found	Calculated
$CH_2I-CH(OCH_3)-CCl=CH_2$	76.5-77	1.7135	1.5312	44.53	44.13
$CH_2I-CH(OC_2H_5)-CCl=CH_2$	82-83	1.6163	1.5220	49.16	48.75
$CH_2I-CH(OCH_3)-CCl=CH-CH_3$	93.5-94.5	1.6355	1.5290	49.13	48.75
$CH_2I-CH(OCH_3)-CCl=CH-C_2H_5$	104-106	1.5267	1.5172	54.42	53.37
$CH_2I-CH(OC_2H_5)-CCl=CH-C_2H_5$	107-109	1.4687	1.5100	58.76	57.99
$CH_2I-CH(OCH_3)-CCl=CH-C_3H_7$	115-117	1.4868	1.5163	58.68	57.99
$CH_2I-CH(OCH_3)-CCl=CH-C_4H_9$	129-133	1.4293	1.5120	63.53	62.60
$CH_2I-CH(OCH_3)-CCl=CH-(CH_2)_2-CH(CH_3)_2$	137-139	1.3930	1.5092	67.86	67.22
$CH_2I-CH(OC_2H_5)-CCl=CH-(CH_2)_2-CH(CH_3)_2$	141-144	1.3486	1.5040	72.60	71.84

Iodoalkoxylation of chloroprene homologs was effected by the action of iodine and mercuric oxides upon their solutions in methyl and in several cases, ethyl alcohol.

The following 6 substances could have been expected as a result of the reaction, of which II and IV were the least probable, since they have never been found in reactions of conjugated systems.

I. $CH_2I-CH(OR)-CCl=CH-R$; II. $CH_2(OR)-CHI-CCl=CH-R$; III. $CH_2=CH-CCl(OR)-CHI-R$;

IV. $CH_2=CH-CClI-CH(OR)-R$; V. $CH_2I-CH=CCl-CH(OR)-R$; VI. $CH_2(OR)-CH=CCl-CHI-R$

The structure of the main parts of the reaction products was proved in the following manner:

1) Propionic acid was obtained by the oxidation of the iodo ether of the chlorohexadiene by a neutral potassium permanganate solution, whereas iodoacetic acid was not present in any quantity in the reaction products. These results forced formulas III, IV, V, and VI to be discarded.

2) Dienic chloroether were obtained from all of the iodoethers by the action of alcoholic alkali, which could be hydrolyzed to unsaturated chloroketones by shaking with dilute acid solutions Therefore, the chloroethers were derivatives of the enol forms of these ketones. These results forced formulas II, III, V, and VI to be discarded. Substances with formula II should have given unsaturated chloroaldehydes with these transformations; substances with formula III, an unsaturated iodoketone or the acetal of the ketone; and finally, substances with formulas V and VI, ethers of unsaturated chloroalcohols. None of the possible reaction products were detected in any sort of a quantity.

Therefore, the iodoethers obtained must be assigned formula I.

Small lower and higher boiling fractions were always obtained in addition to the main substance during the iodoalkoxylation of the chloroprene homologs. They arose, to a great extent, as a result of the fairly strong decomposition of the iodo ethers during distillation. 1,4- Products could be found in the higher boiling fraction, but their quantity was small. If half of the whole residue after separation of the main substance was assigned to the 1,4 products, then their yield would not exceed one tenth that of the main substance In most cases, it was considerably below this value.

Therefore, it was shown that alkyl hypoidites add to chloroprene homologs in the same order as to chloroprene.

The physical properties of the ethers are given in Table 2 along with the corresponding properties of the ethers

The constants are given in Table 2, analytical results in Table 8.

5. Iodomethoxylation of chlorooctadiene. 38 g of a product was obtained from 27 g of the substance, 50 ml of methanol, 30 g of mercuric oxide, and 47 g of iodine. The following fractions were obtained upon distillation of the substance (at 10 mm): 1) up to 120°-3 g, 2) 120-129°-4.5 g, 3) 129-133°-25 g, 4) 133-135°-5 g, 5) residue 2.5 g. Yield of the main fraction48%. The constants are given in Table 2, analytical data in Table 8.

6. Iodomethyoxylation of chloromethyloctadiene. 35 g of an oil was obtained from 22 g of the substance, 60 ml of methanol, 23 g of mercuric oxide and 35.5g of iodine, which gave the following fractions upon distillation (at 10 mm): 1) up to 135°-2.5 g, 2) 135-139°-29.7 g, 3) residue, 2 g. Yield of the main fraction, 68%.

7. Iodoethoxylation of chloromethyloctadiene. 29 g of an oil was obtained from 20 g of the substance, 50 ml of ethyl alcohol, 20 g of mercuric oxide, and 32 g of iodine, which was separated into the following fractions upon distillation: 1) up to 141°-3 g, 2) 141-144°-22g, 3) residue, 2 g. Yield of the main fraction, 60%.

IV. Preparation of Dienic Chloroethers

In order to prepare the dienic chloroethers, the products reported in the previous section were added in small portions to a 25% KOH solution taken in 1.5 excess, heated to boiling. After the addition of all of the substance, the solution was heated for 0.5-1 hour on the oil bath, and the products then steam distilled. The oil collected in the receiver was separated from the water layer, washed with a calcium chloride solution, dried over $CaCl_2$, and vacuum distilled. Yield of the ether based on a 1-2° fraction was 40-50%. Data are given for the distillation of 2-methoxy-3-chloroheptadiene-1,3. 18 g of the substance was obtained from 40 g of the iodoether, which was separated by distillation into the following fractions (at 85 mm): 1) up to 119°-1.8 g, 2) 119-120°-12 g, 3) residue 2.7 g.

The constants of the dienic chloroethers are given in Table 3, the analytical data in Table 8. All of the substances have a specific odor, are insoluble in water, and polymerize if stored.

V. Preparation of Methylalkylchlorovinyl Ketones

All of the ketones were prepared by shaking the dienic chloroethers with 5-6 times the quantity of 5% H_2SO_4 at 40-50°. Methoxychloropentadiene was completely hydrolyzed in 1 hour, methoxychloroheptadiene in 3-4 hours, methoxychlorooctadiene in 6 hours. Methoxychloromethyloctadiene did not react completely in 10 hours. The completion of the reaction was judged by the fact that the refractive index did not change on further shaking with acid.

TABLE 7

Substance	Weight of sample (g)	Weight AgCl + AgI	% Cl + I	
			Found	Calculated
$CH_2I-CH(OCH_3)-CCl=CH-CH_3$	0.1434	0.2072	62.05	62.32
	0.1260	0.1832	62.44	62.32
$CH_2I-CH(OCH_3)-CCl=CH-C_2H_5$	0.1282	0.1759	58.92	59.14
$CH_2I-CH(OC_2H_5)-CCl=CH-C_2H_5$	0.1272	0.1654	55.84	56.27
$CH_2I-CH(OCH_3)-CCl=CH-C_3H_7$	0.1204	0.1566	55.82	56.26
	0.1322	0.1724	56.00	56.26
$CH_2I-CH(OCH_3)-CCl=CH-C_4H_9$	0.1141	0.1414	53.21	53.66
$CH_2I-CH(OCH_3)-CCl=CH-(CH_2)_2-CH(CH_3)_2$	0.1220	0.1448	50.96	51.28
	0.1179	0.1391	50.66	51.28
$CH_2I-CH(OC_2H_5)-CCl=CH-(CH_2)_2-CH(CH_3)_2$	0.1166	0.1320	48.74	49.11
	0.1256	0.1444	49.37	49.11

The yield of the ketones was 50-60% based on the fraction boiling within 0.5-3.0°. The constants of the ketones are given in Table 4, analytical results in Table 9.

The semicarbazones of the ketones were obtained by Zelinsky's method, nitro and dinitrophenylhydrazones, by the usual method in acetic acid; they were recrystallized from alcohol or dilute alcohol. The melting points of these substances are given in Table 4.

The substances did not react with fuchsine sulfurous acid, and therefore, were not aldehydes.

TABLE 8

Substance	Weight of sample (g)	Weight AgCl (g)	% Cl	
			Found	Calculated
$CH_2=C(OCH_3)-CCl=CH-CH_3$	0.1199	0.1298	26.78	26.74
	0.1028	0.1120	26.95	26.74
$CH_2=C(OCH_3)-CCl=CH-C_2H_5$	0.1128	0.1104	24.21	24.18
$CH_2=C(OC_2H_5)-CCl=CH-C_2H_5$	0.1234	0.1084	21.73	22.07
$CH_2=C(OCH_3)-CCl=CH-C_3H_7$	0.1004	0.0880	21.68	22.07
$CH_2=C(OCH_3)-CCl=CH-C_4H_9$	0.1176	0.0961	20.22	20.30
	0.1157	0.0940	20.10	20.30
$CH_2=C(OCH_3)-CCl=CH-(CH_2)_2-CH(CH_3)_2$	0.1054	0.0786	18.45	18.79
	0.1212	0.0892	18.22	13.79
$CH_2=C(OC_2H_5)-CCl=CH-(CH_2)_2-CH(CH_3)_2$	0.1282	0.0914	17.64	17.49

TABLE 9

Substance	Weight of sample (g)	Weight AgCl (g)	% Cl	
			Found	Calculated
$CH_3-CO-CCl=CH-CH_3$	0.1380	0.1630	29.22	29.90
	0.1156	0.1383	29.60	29.90
$CH_3-CO-CCl=CH-C_2H_5$	0.1214	0.1289	26.27	26.75
$CH_3-CO-CCl=CH-C_3H_7$	0.1339	0.1296	23.94	24.18
	0.0974	0.0942	23.92	24.18
$CH_3-CO-CCl=CH-C_4H_9$	0.1224	0.1072	21.66	22.07
	0.1285	0.1108	21.33	22.07
$CH_3-CO-CCl=CH-(CH_2)_2-CH(CH_3)_2$	0.1378	0.1064	19.10	20.30

By bromination of the ketones with the theoretical amount of bromine in chloroform, their bromides were obtained, of which only 1 could be distilled; the rest decomposed with the evolution of hydrogen bromide. Upon reducing them with zinc shavings in 80% acetic acid, in several cases mixtures of saturated and unsaturated ketones were obtained, whose separation into components was not attempted. The chlorobromo ketones were not oxidized in the cold with chromic mixture; this led to the conclusion that they did not contain aldehydes as impurities.

SUMMARY

1. The order of addition of alkyl hypoiodites to homologs of chloroprene was investigated, and several of these homologs were first synthesized.

2. It was shown that alkyl hypoiodites added in the same order as to chloroprene, predominantly to the unsubstituted double bond.

3. A series of dienic chloroethers was obtained by the action of alcoholic alkalies upon the chloroethers: 2-methoxy-3-chloropentadiene-1,3, 2-methoxy-3-chlorohexadiene-1,3, 2-ethoxy-3-chlorohexadiene-1,3, and others.

4. A series of methylchlorovinyl ketones was obtained by hydrolytic cleavage of these ethers. 3-Chloropenten-3-one-2, 3-chlorohexen -3-one-2, and others.

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REACTIONS OF ETHER OXIDES WITH NITROGEN COMPOUNDS

VI. REACTION OF METHYL AND ETHYL GLYCIDE ETHERS WITH DIETHYLAMINE

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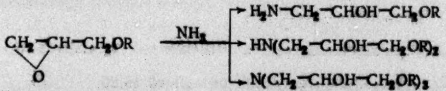
In the previous communication [1] it was shown that methyl and ethyl glycide ethers reacted quite energetically with ammonia (in contrast to amides) [2-4] even at room temperature with the formation of the corresponding ethers of aminopropanediol:


CH_2—CH—CH_2OR
O
NH_3
H_2N—CH_2—CHOH—CH_2OR
HN(CH_2—CHOH—CH_2OR)$_2$
N(CH_2—CHOH—CH_2OR)$_3$

The present communication reports the results of experiments on the reaction of methyl and ethyl glycide ethers with diethylamine.

The reaction of methyl glycide ether with diethylamine has not been reported in the literature, while the reaction of ethyl glycide ether with secondary amines is only mentioned slightly [5].

Experiments showed that glycide ethers react readily with aqueous solutions of diethylamine to form the expected ethers of diethylaminopropanediol:

$(C_2H_5)_2N-CH_2-CHOH-CH_2OCH_3$ (I); $(C_2H_5)_2N-CH_2-CHOH-CH_2OC_2H_5$. (II)

In the absence of water, these substances do not noticeably react at usual or elevated (80°) temperatures.

Heating greatly accelerates the reaction with the aqueous amine so that the yield of the diethylaminopropanediol ethers is only slightly smaller after a 3 hour heating on the boiling water bath then after 72 hours standing at room temperature. Further increase of the temperature to 125-130° and of the heating time to 6 hours did not give better results.

The reagents were taken in a ratio of 1 mole of the ether to 2 or 3 moles of diethylamine. Under these conditions the reaction proceeded only in the direction of the formation of aminopropanediol ethers (I) and (II), and is not accompanied by side processes. The reaction with glycide ethers proceeds at approximately the same rate as with propylene oxide [6] and considerably greater than with trimethylethyl oxide [7].

Ethers of aminopropanediol (I) and (II) which were obtained are colorless liquids with basic properties, less hygroscopic than the corresponding products obtained by the reaction of the same ethers with ammonia [1].

The presence of hydroxyl groups in the aminoalcohols (I) and (II) was proved by acetylation with acetic anhydride Picrates were obtained from both bases, and in addition, an ethiodide was obtained for amine (I).

EXPERIMENTAL

Glycide ethers were obtained from glycerine α-monochlorohydrin ethers [8-15]. 1.2 mole of powdered potassium hydroxide, 250 ml of absolute ether, were placed into a round-bottom flask with a reflux condenser, and 1 mole of purified glycerine chlorohydrin was added over a 1.5 hour period through the condenser in small portions with shaking. A slight heating occurred. The mixture was heated for 1 hour to 50-60° on the water bath, the residue was then separated, washed with 3 times with 30 ml of dry ether, the ether was removed on the water bath, and the product distilled through a three ball dephlegmator. The yield of glycide methyl ether was 65%, the ethyl, 62%.

Reaction of Glycide Methyl Ether with Diethylamine. Synthesis of 3-methoxypropanol-2-diethylamine (I) (together with E. F. Parinova).

a) 37 g (0.5 moles) of diethylamine (b.p. 56-57°) in 75 ml of water was added with shaking to 15 g (0.17

mole) of glycide methyl ether (b.p. 110-112°, n_D^{20} 1.4042). A homogenous colorless liquid was obtained upon mixing the reagents, and the temperature rose from 20-60° (if the mixture was not cooled with water).

After heating the mixture for 3 hours on the boiling water bath, the amino alcohol formed was salted out with potassium hydroxide, separated (upper layer), dried with KOH, and vacuum distilled. 21.5 g (78.4%) of 3-methoxypropanol-2-diethylamine (I) was obtained. The yield here and subsequently was calculated on the basis of the glycide ether.

In two other analogous experiments in which the heating was continued for 5 hours at 125-130° on the oil bath, 65 and 68% of product (I) was obtained.

b) 68.5 g (0.9 mole) of diethylamine in 134 ml of water was added to 29.2 g (0.33 mole) of the methyl ether, and the mixture allowed to stand at room temperature for 72 hours. As a result of the processing of the product analogously to the previous experiment, 30.9 g (58%) of the aminopropanediol ether (I) was obtained. If the amount of 33% amine was decreased from three to two moles per mole of ether, and the time of standing from 72 to 66 hours, the yield of the product fell to 44%.

3-Methoxypropanol-2-diethylamine had the following constants after redistillation in vacuum:

B.p. 75-77° at 6 mm; d_4^{20} 0.9221; n_D^{20} 1.4390; MR_D 45.95; calculated 46.25.

0.1449 g substance: 8.86 ml 0.1 N H_2SO_4 (according to Kjeldahl). 0.1272 g substance: 7.72 ml 0.1 N H_2SO_4. 0.1410 g substance: 0.2034 g AgI (according to Zeisel). 0.1968 g substance: 11.81 ml 0.1 N NaOH. 0.3470 g substance: 26.48 g benzene: Δt 0.41°. 0.4370 g substance: 26.48 g benzene: Δt 0.52°. Found %: N 8.56, 8.49; CH_3O 19.04; OH 10.19; M 163.02, 161.9. $C_8H_{19}O_2N$. Calculated %: N 8.69; CH_3O 19.24; OH 10.54; M 161.2.

The aminoalcohol ether obtained was a colorless liquid with a weak amine odor, which yellowed slightly upon standing. It did not distill at atmospheric pressure without decomposition. It was readily soluble in alcohol, ether, and dioxane, poorly in cold, and more so in hot water. It rapidly decolorized a chloroform solution of bromine and potassium permanganate. It reacted with metallic sodium. It kept unchanged for a long time in closed vessels. It absorbed moisture under usual conditions in the air. A sample of 0.9718 g gave a weight increase of 1.6% after 6 hours.

The picrate of this aminoalcohol, obtained by mixing equimolecular amounts of alcoholic solutions of the base and picric acid, was a lemon yellow crystalline substance which melted at 163° after two recrystallizations from water. The picrate was analyzed in the manner reported previously [1].

0.1020 g substance: 10.1 ml 0.1 N H_2SO_4. 0.1131 g substance: 11.23 ml 0.1 N H_2SO_4. Found %: N 13 86, 13.90. $C_{14}H_{22}O_9N_4$. Calculated %: N 14.35.

The ethiodide of base (I) was obtained by mixing solutions of equimolecular amounts of the reagents in absolute ether. Washed many times with ether, the ethiodide melted at 96-97°. Colorless crystals, readily soluble in water and alcohol.

0.1942 g substance: 6.11 ml 0.1 N $AgNO_3$. 0.1168 g substance: 3.70 ml 0.1 N $AgNO_3$. 0.1578 g substance: 4.94 ml 0.1 N H_2SO_4. 0.1440 g substance: 4.44 ml 0.1 N H_2SO_4. Found %: I 39.93, 40.20; N 4.38, 4.31. $C_{10}H_{24}O_2NI$. Calculated %: I 40.01; N 4.41.

The aminoalcohol hydrochloride was obtained by the evaporation of a solution of the product in dilute hydrochloric acid on the water bath, and was a viscous, noncrystallizing mass.

The aminoalcohol acetate was obtained by the action of acetic anhydride on the propanediol ether (I) in the presence of a drop of sulfuric acid. It was a colorless liquid with a specific odor.

B.p. 82-84° at 8 mm; d_4^{20} 0.9817; n_D^{20} 1.4340; MR_D 54.10; calculated 55.61. 0.1376 g substance: 6.78 ml 0.1 N H_2SO_4. 0.1211 g substance: 6.04 ml 0.1 N H_2SO_4. Found %: N 6.89, 6.98; $C_{10}H_{21}O_3N$. Calculated %: N 6.89.

The acetate was readily soluble in water, alcohol, and insoluble in benzene.

The aminoalcohol (I) obtained did not give a crystalline derivative with gold chloride.

Reaction of Glycide Ethyl Ether with Diethylamine. Synthesis of 3-Ethoxypropanol-2-diethylamine (II) (together with A. V. Zlobina)

a) 36.5 g of freshly distilled diethylamine was added to 17 g (~0.17 mole) of glycide ethyl ether (b.p. 124-126°, n_D^{20} 1.4080). Heating occurred upon mixing (the temperature rose from 18-55°). When heated on the boiling water bath, the reaction mixture was first homogenous, and then separated into two layers after 15-20 minutes. The upper, which was the aminoalcohol (II), was separated after heating for 3 hours, another small layer was formed by saturating the water solution with potassium hydroxide (KOH), which was combined with the initially separated one, dried with solid potassium hydroxide, and was vacuum distilled. 24 g (80%) of 3-ethoxypropanol-2-diethylamine (II) was obtained.

In two analogous experiments, but with heating on an oil bath at 125-130°, 62.9% of the reaction product was obtained by a 5 hour heating, and 56% after 1 hour heating.

b) 33.6 g (0.46 mole) of diethylamine in 69 ml of water was added to 23.5 g (0.23 mole) of the ether, and the mixture was allowed to stand at room temperature for 72 hours. After the corresponding processing and vacuum distillation, 22.9 g (57%) of 3-ethoxypropanol-2-diethylamine was obtained. This aminoalcohol was obtained in a yield of 48% of theory as a result of 2 hours standing at room temperature and an initial energetic 30 minute shaking.

The 3-ethoxypropanol-2-diethylamine obtained had the following constants after redistillation:

B.p. 84-85° at 6 mm; d_4^{20} 0.9100; n_D^{20} 1.4390; MR_D 50.25; calculated 50.87.

0.1008 g substance: 5.69 ml 0.1 N H_2SO_4 (according to Kjeldahl). 0.1198 g substance: 6.03 ml 0.1 N H_2SO_4. 0.1964 g substance: 0.2597 g AgI (according to Zeisel). 0.1882 g substance: 10.25 ml 0.1 N NaOH. 0.1074 g substance; 22.82 g benzene: Δt 0.17°. 0.1152 g substance: 22.82 g benzene: Δt 0.126°. Found %: N 7.90, 7.88; C_2H_5O 25.40; OH 9.26; $M_{av.}$ 174.7. $C_9H_{21}O_2N$. Calculated %: N 7.99; C_2H_5O 25.70; OH 9.70; M 175.26.

The colorless liquid with a weak odor of amine, which yellowed slightly on standing, had an alkaline reaction and a bitter burning taste. It did not distill at ordinary pressure without decomposition. It was readily soluble in alcohol, ether, and dioxane, poorly, in cold and more so in hot water. It rapidly decolorized a chloroform solution of bromine and a potassium permanganate solution, reacted with metallic sodium. It absorbed moisture under the usual conditions. A sample of 0.9763 g of the substance gave weight increase of 1.5% after 6 hours.

The picrate of the aminoalcohol was a light yellow crystalline substance with m.p. 83° (from water).

0.1203 g substance: 11.03 ml 0.1 N H_2SO_4. 0.1152 g substance: 10.41 ml 0.1 N H_2SO_4. Found %: N 12.84, 12.65. $C_{15}H_{24}O_9N_4$. Calculated %: N 13.85.

The picrate contained less nitrogen then required by theory. Apparently, it crystallized with two molecules of water which were stably held and were not given off even upon prolonged standing in a desiccator over H_2SO_4 and upon heating in a drying cabinet at 80-90°.

The ethiodide of the base precipitated in the form of a non-crystallizing oil.

The chloroaurate of the base gave a lower per cent of gold upon analysis. It could not be purified any further.

The acetate of the aminoalcohol, obtained under the same conditions as the acetate of aminoalcohol (I), was a colorless liquid with a specific odor; it was readily soluble in water, alcohol, and ether.

B.p. 95-97° at 8 mm d_4^{20} 0.9420; n_D^{20} 1.4370; MR_D 60.39; calculated 60.24. 0.1165 g substance: 4.50 ml 0.1 N H_2SO_4 (according to Kjeldahl). 0.1062 g substance: 4.16 ml 0.1 N H_2SO_4. Found %: N 5.41, 5.48. $C_{11}H_{23}O_3N$. Calculated %: N 6.44.

The acetate was not completely pure and contained a lower percent of nitrogen than required by theory. It could not be purified any further.

SUMMARY

1. The reaction of glycide methyl and ethyl ethers with aqueous diethylamine was studied.

2. The following products of these reactions were obtained and characterized: 3-methoxypropanol-2-diethylamine, 3-ethoxypropanol-2-diethylamine, their acetates and several salts.

3. It was shown that glycide ether resembles propylene oxide in activity and reaction with diethylamine, and are considerably more active then trimethylethylene oxide.

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* See Consultants Bureau Translation, p. 681.

** See Consultants Bureau Translation, p. 2135.

*** See Consultants Bureau Translation, p. 151.

**** See Consultants Bureau Translation, p. 985.

CONDENSATION PRODUCTS OF TRIARYLCARBINOL WITH 1-PHENYL-3-METHYLPYRAZOLONE-5

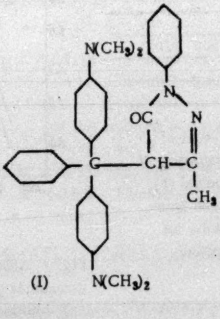
O. F. Ginzburg and V. R. Terushkin

As is known, triphenylcarbinol possesses a very labile hyrdroxyl group, and its basic properties are expressed to a considerable extent [1]. The basic properties are expressed to a greater extent in derivatives of triphenylcarbinol containing a substituent of the primary type in the para position to the central carbon atom. Especially active are the hydroxyl groups in carbinol compounds obtained from the basic triphenylmethane dyes, which is expressed, in particular, in reaction of these substances with compounds containing labile hydrogen atoms and methyl and methylene groups. It is known, for example, that triphenylcarbinol itself reacts with malonic ester to form triphenylmethylmalonic ester [2]. Recently, A. N. Nesmeyanov and coworkers showed that 4,4',4"-hexamethyltriaminotriphenylcarbinol or its methyl ether participates in a condensation reaction with nitromethane and aliphatic aldehydes to form compounds in which the tris(p-dimethylaminophenyl)methyl radical bound to the aldehyde or nitromethane residue is very labile [3].

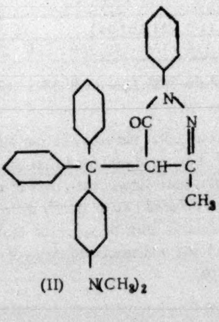
In the present investigation, it was decided to examine the ability of several carbinol compounds and their methyl ethers to participate in condensation reactions with 1-phenyl-3-methylpyrazolone-5 which, as is known, contains very active hydrogen atoms.

The experiments conducted showed that 4,4'-tetramethyldiaminodiphenylcarbinol, 4,4'-tetramethyldiaminotriphenylcarbinol, and its methyl ether, as well as 4-dimethylaminotriphenylcarbinol methyl ether readily participate in condensation reactions with 1-phenyl-3-methylpyrazolone-5. Thus, for example, even upon heating the above compounds with 1-phenyl-3-methylpyrazolone-5 in methyl alcohol, lightly colored condensation products are formed which gradually precipitate from the solution. Upon heating 4,4',4"-hexamethyltriaminotriphenylcarbinol with 1-phenyl-3-methylpyrazolone-5 in methyl alcohol, only an intensely violet colored solution forms from which, however, the reaction product does not precipitate.

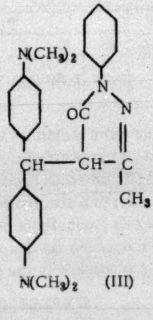
A study of the properties, as well as the analysis of the products obtained showed that these substances possess the following structures:



(I)



(II)

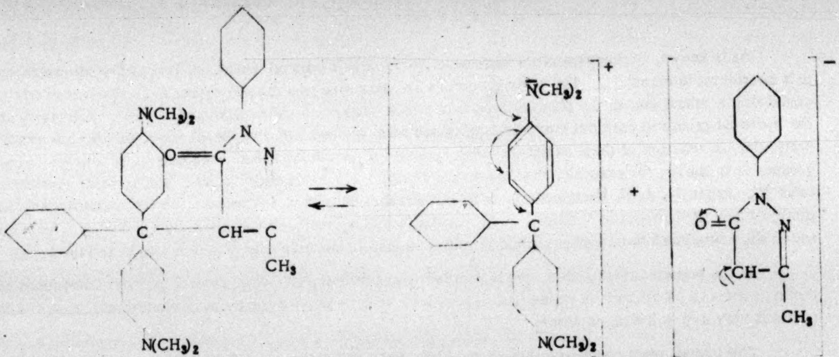


(III)

It must be mentioned that, under the above conditions, triphenylcarbinol does not participate in a condensation reaction with 1-phenyl-3-methylpyrazolone-5 because of the insufficient basicity of triphenylcarbinol.

The compounds synthesized have the ability to dissolve in aqueous alcoholic alkali solutions because of the presence of the 1-phenyl-3-methylpyrazolone-5 residue in them, from which they are precipitated by careful acidification with acetic acid. These compounds, like the products of the condensation of 4,4',4"-hexamethyltriaminotriphenylcarbinol with aliphatic aldehydes and nitromethane, reported by A. N. Nesmeyanov and coworkers [3], are subjected to acidolysis. Thus for example, solutions of the color of the corresponding dye are formed by the action of acetic acid. However, the decomposition of these compounds also occurs upon solution in certain aprotic polar solvents

Thus for example, a solution of color corresponding to the dye is formed by dissolving compounds (II) and (III) in nitrobenzene, while compound (I) decomposes not only in nitrobenzene, but also in chloro- and bromobenzene. As an example, absorption spectra of malachite green and compound (I) in nitrobenzene are given in Fig. 1. Comparison of these absorption curves shows their identity. Thus, since the color of solutions of malachite green is caused by the presence of cations of the dye, therefore, compound (I) has these same cations in nitrobenzene. The dissociation of compounds (I), (II), and (III) into ions occurs in the same manner in a series of polar solvents, and the dissociation, for example, of compound (I) may be described by the following equations:



More detailed study of nitrobenzene solutions of compounds (I) and (II) showed that the dissociation of these compounds is not complete. The degree of dissociation of compound (I) in nitrobenzene was calculated by the determination of the concentration of dye cations in the nitrobenzene solution of known concentration of compound (I) from the intensity of absorption. Measurement of the intensity of absorption of the same nitrobenzene solution of compound (I) at various intermediate times showed that its dissociation in nitrobenzene proceeds comparatively slowly. Data characterizing the change of the degree of dissociation with time of compound (I) in nitrobenzene solution is given below, where the time is given from the moment of the first measurement.

TABLE 1

Change of the Degree of Dissociation of Compound (I)

Degree of dissociation	Time (in minutes)											
	00	30	57	89	119	149	180	209	239	279	300	1202
a %	3.83	5.30	6.11	7.76	8.56	9.73	11.0	11.9	13.1	13.5	14.0	19.4

The same picture is also found upon the study of the dissociation of Compound (II) in nitrobenzene. It must be mentioned that the dissociation of compound (II) proceeds considerably more slowly than that of compound (I) (Fig. 2). Since the accumulation of colored cation in the nitrobenzene solutions decreases gradually in both cases, it must be supposed that finally, an equilibrium between the dissociated and undissociated parts of compounds (I) and (II) is reached in the solution.

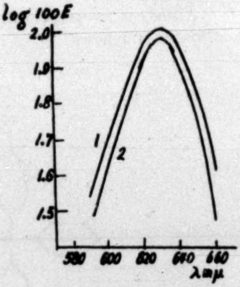


Fig. 1. Absorption spectra of malachite green hydroiodide and compound (I).
1) The hydroiodide; 2) compound (I).

EXPERIMENTAL

I. 4,4'-Tetramethyldiaminotriphenyl-(1-phenyl-3-methylpyrazolone-5-yl-4)methane (compound I)

a) 5.00 g of 4,4'-tetramethyldiaminotriphenylcarbinol methyl ether was added to a solution of 7.50 g of 1-phenyl-3-methylpyrazolone-5 in 40 ml of methyl alcohol, and the mixture was refluxed for 4 hours in a flask. After cooling, the precipitate was filtered, thoroughly washed with alcohol and benzene, and dried in a vacuum desiccator over potassium hydroxide. The compound obtained melted with decomposition at 162-165°. Yield 6.37 g or 91.4% of the theoretical based on malachite green methyl ether.

TABLE 2

$c \cdot 10^6$ moles/liter	E	$K \cdot 10^{-5}$
0.50	0.4007	1.60
1.25	1.0069	1.61

TABLE 4

$c \cdot 10^6$ moles/liter	E	$K \cdot 10^{-4}$
3.45	0.4204	2.44
4.32	0.5040	2.50
5.18	0.6430	2.48
6.05	0.7528	2.50
6.90	0.9020	2.62
8.35	1.0201	2.44
8.64	1.1093	2.58

TABLE 3

Time (min.)	E	Cation conc. $x \cdot 10^6$ moles/liter	α %
00	0.2495	0.306	3.83
30	0.3408	0.424	5.30
57	0.3934	0.489	6.11
89	0.4988	0.620	7.76
119	0.5918	0.686	8.56
149	0.6252	0.778	9.73
180	0.7097	0.884	10.99
209	0.7636	0.949	11.87
239	0.8412	1.046	13.09
279	0.8730	1.086	13.59
300	0.8997	1.119	13.88
1202	1.2447	1.550	19.40

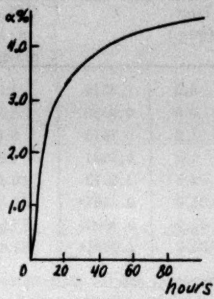


Fig. 2. Change of the degree of dissociation. (of II).

b) 0.5 g of 4,4'-tetramethyldiaminotriphenylcarbinol was added to a solution of 0.75 g of 1-phenyl-3-methylpyrazolone-5 in 20 ml of methyl alcohol. The solution obtained was refluxed for 2 hours. After cooling the precipitate was filtered, thoroughly washed with alcohol and benzene, and dried in a drying chamber at 80°. The compound obtained melted with decomposition at 162-165°. Yield 0.46 g or 66.3% of the theoretical based on 4,4'-tetramethyldiaminotriphenylcarbinol.

0.1424 g substance: 0.4105 g CO_2; 0.0905 g H_2O. 0.0637 g substance: 6.20 ml N_2 (22°, 761 mm). 0.0778 g substance: 7.81 ml N_2 (24°, 758 mm). Found %: C 78.62; H 7.11; N 11.20, 11.40. $C_{33}H_{34}ON_4$. Calculated %: C 78.84; H 6.82; N 11.14.

Determination of the absorption coefficient of a nitrobenzene solution of malachite green hydroiodide. All of the spectrophotometric measurements were effected on the Koenig-Martens spectrophotometer. Malachite green hydroiodide was prepared by the decomposition of 4,4'-tetramethyldiaminotriphenylcarbinol methyl ether with methyl magnesium iodide. A solution of malachite green hydroiodide in nitrobenzene was prepared and intensity of absorption E of these solutions at λ = 630 mμ and 5 cm layer thickness was measured. The absorption coefficient was calculated on the basis of the data obtained (Table 2).

Determination of the degree of dissociation of 4,4'-tetramethyldiaminotriphenyl-(1-phenyl-3-methylpyrazolone-5-yl-4)-methane in nitrobenzene. A sample of compound (I) was ground with a small amount of nitrobenzene, and the mixture was washed into a 50 ml volumetric flask. The contents of the flask were shaken until complete solution of compound (I), and the solution was brought to the mark; then a solution was prepared by subsequent dilution, the concentration of which was $8 \cdot 10^{-6}$ moles / liter. The intensity of absorption of the solution was measured periodically at λ = 630 mμ, and 5 cm layer thickness. The recording of the time is given from the moment of the first measurement. The solution was kept at 21 ±0.5°. The absorption coefficient from the data of Table 2 was taken to be equal to $1.60 \cdot 10^5$. The results obtained are given in Table 3.

II. 4-Dimethylaminotriphenyl-(1-phenyl-3-methylpyrazolone-5-yl-4)-methane (Compound II)

2.30 g of 4-dimethylaminotriphenylcarbinol methyl ether was added to a solution of 1.27 g of 1-phenyl-3-methylpyrazolone-5 in 50 ml of methyl alcohol, and the mixture obtained was refluxed for 6 hours in a flask. The solution was colored red, and a voluminous precipitate formed at the end of the heating. On the following day, the residue was filtered, thoroughly washed with alcohol and benzene, and dried in a drying cabinet at 85°. 2.61 g of a product with m.p. 179-180° was obtained. Yield 77.5% of the theoretical based on the starting methyl ether of 4-dimethylaminotriphenylcarbinol.

0.1402 g substance: 0.4147 g CO_2; 0.0824 g H_2O. 0.0899 g substance: 7.40 ml N_2 (21°, 757 mm). 0.0698 g substance: 5.86 ml N_2 (22°, 763 mm). Found %: C 80.67; H 6.57; N 9.46, 9.64. $C_{32}H_{29}ON_3$. Calculated: C 81.00; H 6.36; N 9.48.

TABLE 5

Time (min.)	E	Cation conc. $x \cdot 10^6$ moles/liter	α %
0.0	0.4519	3.65	0.20
0.5	0.5583	4.50	0.25
1.2	0.7618	6.15	0.34
1.8	0.9531	7.69	0.42
2.5	1.2613	10.30	0.57
31.0	0.8363*	67.5	3.73
55.0	0.9602*	77.5	4.29
101.0	1.0291*	82.6	4.56

Determination of the absorption coefficient of a nitrobenzene solution of 4-dimethylaminotriphenylcarbinol picrate. A series of solutions of 4-dimethylaminotriphenylcarbinol picrate in nitrobenzene were prepared and the intensity of absorption E for these solutions was measured at λ = 500 mμ, and 5 cm layer thickness. The absorption coefficient K was calculated on the basis of the data obtained. The solution of the picrate in nitrobenzene was effected in red light (Table 4).

Determination of the degree of dissociation of 4-dimethylaminotriphenyl-(1-phenyl-3-methylpyrazolone-5-yl-4)-methane in nitrobenzene. A weighed sample of compound (II) was ground with a small amount of nitrobenzene, and the mixture washed into a volumetric flask. The contents of the flask were shaken until complete solution of the compound (II). A solution was prepared by subsequent dilution, whose concentration was equal to $1.81 \cdot 10^{-3}$ moles/liter. The preparation of the solution was effected in red light. The intensity of absorption was measured periodically at λ = 500 mμ and 5 cm layer thickness. The recording of the time was started from the moment of the first measurement. The solution was kept at 21 ±0.5°. The absorption constant was taken to be equal to $2.50 \cdot 10^4$ from the data in Table 4. The data obtained are given in Table 5.

III. 4,4'-Tetramethyldiaminodiphenyl-(1-phenyl-3-methylpyrazolone-5-yl-4)-methane (Compound III)

1.00 g of 4,4'-tetramethyldiaminodiphenylcarbinol and 0.68 g of 1-phenyl-3-methylpyrazolone-5 were dissolved in 30 ml of methyl alcohol. The solution was refluxed for 2 hours on the water bath in a flask. On the following day, the precipitate which formed was filtered, thoroughly washed with alcohol, and dried in a drying cabinet at 90°. The substance melted with decomposition at 193-194°. The melting point did not change after recrystallization from alcohol. The compound obtained was identical with 4,4'-tetramethyldiaminodiphenyl-(1-phenyl-3-methylpyrazolone-5 yl-4)-methane synthesized by Kehlstadt [4].

SUMMARY

The 4,4'-tetramethyldiaminodiphenylcarbinol, the methyl ether of the 4-tetramethyldiaminotriphenylcarbinol, the 4,4'-tetramethyldiaminotriphenylcarbinol, and its methyl eter condense readily with 1-phenyl-3-methylpyrazolone. When dissolved in polar solvents, the products of condensation dissociate into ions, and the cations formed are identical to those formed by the corresponding dyes dissolved in the same solvents.

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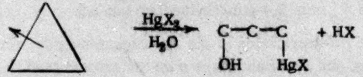
*Before the determination the solution is diluted 10 times.

REACTION OF CYCLOPROPANE HYDROCARBONS WITH SALTS OF MERCURIC OXIDE

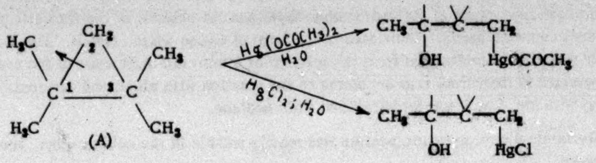
II. NEW ORGANO-MERCURY COMPOUNDS FROM 1,1,2,2-TETRAMETHYLCYCLOPROPANE

R. Ya. Levina and V. N. Kostin

In the previous communication [1] one of the authors (together with B. M. Gladshtein) disclosed the discovery of a reaction opening the three membered ring under the action of salts of mercuric oxide.


HgX_2
H_2O
C—C—C
OH
HgX
+ HX

The reaction of 1,1,2,2-tetramethylcyclopropane (A) with mercuric acetate and chloride in aqueous solution was studied; a detailed investigation of the reaction products showed that the opening of the ring occurs between alkylated and the unalkylated carbon atoms (upon link 1,2) and leads to the formation of 3-hydroxy-2 2 3-trimethylbutyl mercuric acetate (I) and 3-hydroxy-2,2,3-trimethylbutyl mercuric chloride (II) respectively:

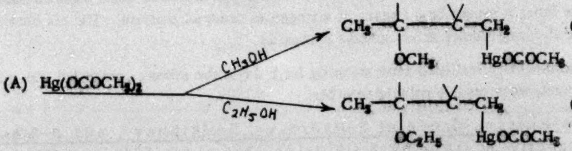

H_3C
CH_2
CH_3
H_3C
CH_3
1
2
(A)
$Hg(OCOCH_3)_2$
H_2O
$HgCl_2; H_2O$
CH_3—C—C—CH_2
OH
$HgOCOCH_3$
CH_3—C—C—CH_2
OH
HgCl

(I)

(II)

Therefore, this reaction is a method for the synthesis of a new type of compound, γ-mercurated alcohols, whose preparation can serve as a method of identification of the cyclopropane series of hydrocarbons.

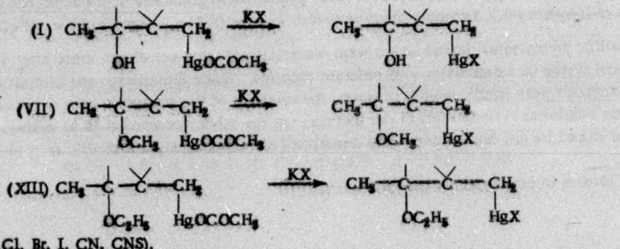
In the present investigation, the method for the preparation of 3-hydroxy-2,2,3-trimethylbutyl mercuric acetate (I) was improved, and the corresponding methoxy and ethoxy compounds were obtained by the reaction between 1,1,2,2-tetramethylcyclopropane with mercuric acetate in methanol and ethanol: 3-methoxy-2,2,3-trimethylbutyl mercuric acetate (VII) and 3-ethoxy-2,2,3-trimethylbutyl mercuric acetate (XIII).


(A) $Hg(OCOCH_3)_2$
CH_3OH
C_2H_5OH
CH_3—C—C—CH_2
OCH_3
$HgOCOCH_3$
CH_3—C—C—CH_2
OC_2H_5
$HgOCOCH_3$

(VII)

(XIII)

Each of the acetates obtained (I, VII, XIII) was transformed by the action of potassium chloride, bromide, iodide, cyanide, and thiocyanate (with cooling and using equimolecular amounts of the reacting substances) into the chloride, bromide, iodide, cyanide, and thiocyanate, respectively:


(I) CH_3—C—C—CH_2
OH
$HgOCOCH_3$
KX
CH_3—C—C—CH_2
OH
HgX
(VII) CH_3—C—C—CH_2
OCH_3
$HgOCOCH_3$
KX
CH_3—C—C—CH_2
OCH_3
HgX
(XIII) CH_3—C—C—CH_2
OC_2H_5
$HgOCOCH_3$
KX
CH_3—C—C—CH_2
OC_2H_5
HgX

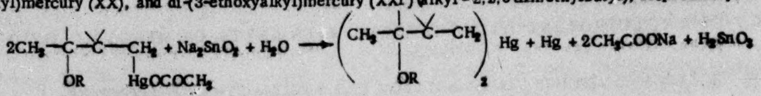
(II–VI)

(VIII–XII)

(XIV–XVIII)

(where X = Cl, Br, I, CN, CNS).

The action of a symmetrical agent, an alkaline solution of sodium stannite, upon 3-hydroxy-, 3-methoxy-, and 3-ethoxyalkyl mercuric acetate resulted in the preparation of di-(3-hydroxyalkyl) mercury (XIX), di-(3-methoxyalkyl)mercury (XX), and di-(3-ethoxyalkyl)mercury (XXI) (alkyl = 2,2,3-trimethylbutyl), respectively.



$$2CH_3-\underset{OR}{\overset{|}{C}}-\overset{\vee}{C}-\underset{HgOCOCH_3}{CH_2} + Na_2SnO_2 + H_2O \longrightarrow \left(CH_3-\underset{OR}{\overset{|}{C}}-\overset{\vee}{C}-CH_2\right)_2 Hg + Hg + 2CH_3COONa + H_2SnO_3$$

(where R = H, CH_3, C_2H_5).

All of the organo-mercury compounds obtained are being reported for the first time, with the exception of (I) and (II) which were reported in the previous communication.

EXPERIMENTAL

1,1,2,2-Tetramethylcyclopropane (b.p. 75.2° at 750 mm, n_D^{20} 1.4003; d_4^{20} 0.7185) was obtained by a method previously developed by the authors [2] from 2,4-dimethylpentadiene-1,3.

Below are given methods for the preparation of the new organo-mercury compound from tetramethylcyclopropane; their yields, melting points, and analyses for the mercury content (and in isolated cases for carbon, hydrogen, and nitrogen) are given in the Table.

Preparation of 3-Hydroxy-2,2,3-trimethylbutyl Mercuric Acetate (I)

12.8 g of tetramethylcyclopropane was added to a filtered solution of 41.6 g of mercuric acetate in 150 ml of distilled water. The reaction mixture was left to stand for 6 days (in a closed bottle) at −5° with periodic shaking. At the end of the reaction (disappearance of the hydrocarbon layer and the absence of the mercuric salt in the solution), the organo-mercury compound partially separated in the form of coarse white crystals. The larger part of the water (4/5 of the volume) was vacuum distilled from the solution at 5 mm; the main mass of the crystals (not containing impurities of mercuric or mercurous salts according to the reaction with alkali and ammonia) came out of the residue upon cooling with ice, which was recrystallized from heptane.

3-Hydroxy-2,2,3-trimethylbutyl mercuric acetate was readily soluble in the cold in ether, acetic acid, chloroform, dioxane, and acetone.

Preparation of 3-Methoxy- and 3-Ethoxy-2,2,3-trimethylbutyl Mercuric Acetates (VII) and (XIII)

The reaction between tetramethylcyclopropane (6.6 g) and a solution mercuric acetate (20.8 g) in absolute methyl alcohol (200 ml), as well as in absolute ethyl alcohol (630 ml*), was effected with the same method used above for the preparation of preparation (I). The reaction time was 3 days. After the removal of the alcohol in vacuum from each reaction mixture, a viscous oil remained which was dissolved once more in absolute ether, the solution filtered, and the ether removed in a stream of nitrogen at reduced pressure. The oil obtained was dried in a desiccator over fused calcium chloride or phosphorus pentoxide.

The methoxy compound crystallized after standing for 2 days; the ethoxy compound was a non-crystalline viscous oil. Both compounds were readily soluble in ether.

Substitution of the Acetate Group of 3-Hydroxy-, 3-Methoxy-, and 3-Ethoxy-2,2,3-trimethylbutyl Mercuric Acetate by a Chloride, Bromide, Iodide, and Cyanide and Thiocyanate Group [3]

A cooled aqueous solution (20 ml) of an equimolecular amount of potassium chloride (0.75 g), or bromide (1.19 g), iodide (1.66 g), cyanide (0.65 g), and thiocyanate (0.97 g) was added gradually with continuous stirring to an ice cooled solution of 3-hydroxy-2,2,3-trimethylbutylmercuric acetate (3.74 g, 0.01 mole) in water (150 ml).

In all cases crystalline precipitates formed which were recrystallized from petroleum ether after washing with water and alcohol, and drying in a desiccator over calcium chloride. Since 3-methoxy- and 3-ethoxy-2,2,3-trimethylbutyl mercuric acetates were poorly soluble in water, the solutions of the potassium salts were added with continuous stirring to water emulsions (110-150 ml) of the methoxy- or the ethoxy-compound (0.01 mole); the reaction mixture was then stirred for 3-4 hours more. The 3-methoxy and 3-ethoxyalkyl mercuric salts obtained

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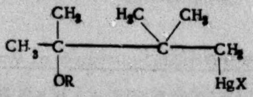
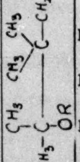
* Mercuric acetate is less soluble in ethyl alcohol than in methyl.

Organo-Mercury Compounds of the Structure



Expt.	R	X	Substance (Alkyl = 2,2,3-trimethylbutyl)	M.p. (°C)	Yield (in % of the theoretical)	Analysis			
						Weight of sample (g)	HgS(g)	Hg (in %)	
								Found	Calc.
I	H	$OCOCH_3$	3-Hydroxyalkyl mercuric acetate	69-70	64	0.3458	0.2154	53.71	53.55
II	H	Cl	" " chloride	116.[illegible]-117	92	0.3147	0.2084	57.10	57.13
						0.3215	0.2190	57.12	–
III	H	Br	" " bromide	123.5-124.5	90	0.2924	0.1722	50.78	50.70
						0.3005	0.1772	50.84	–
IV	H	I	" " iodide	102-102.5	85	0.2514	0.1722	45.37	45.32
						0.2613	0.1336	45.70	–
V	H	CN	" " cyanide *	95.5-96	96	0.2465	0.1677	58.66	58.72
						0.2543	0.1731	58.69	–
VI	H	CNS	" " thiocyanate	73-73.5	93	0.3244	0.2067	53.70	53.68
						0.3152	0.1956	53.51	–
VII	CH_3	$OCOCH_3$	3-Methoxyalkyl mercuric acetate	31.5-32	71	0.3103	0.1844	51.24	51.62
						0.3032	0.1803	51.44	–
VIII	CH_3	Cl	" " chloride	103-103.5	90	0.3310	0.2098	54.65	54.94
						0.3143	0.1994	54.70	–
IX	CH_3	Br	" " bromide	133-133.5	91	0.3458	0.1956	48.77	48.97
						0.3269	0.1844	48.63	–
X	CH_3	I	" " iodide	147-147.5	85	0.2844	0.1446	43.84	43.93
						0.2645	0.1341	43.71	–
XI	CH_3	CN	" " cyanide	53-54	90	0.3005	0.1979	56.81	56.41
						0.3140	0.2062	56.64	–
XII	CH_3	CNS	" " thiocyanate	91-91.5	85	0.3341	0.2010	51.90	51.74
						0.3298	0.1975	51.64	–
XIII	C_2H_5	$OCOCH_3$	3-Ethoxyalkyl mercuric acetate	Oil	56	0.2148	0.1241	49.81	49.82
						0.2312	0.1330	49.60	–
XIV	C_2H_5	Cl	" " chloride	58.5-59	75	0.2403	0.1467	52.64	52.91
						0.2269	0.1392	52.90	–
XV	C_2H_5	Br	" " bromide	61-61.5	72	0.2108	0.1160	47.45	47.35
						0.2255	0.1239	47.37	–
XVI	C_2H_5	I	" " iodide	66-66.5	70	0.2351	0.1161	42.48	42.62
						0.2041	0.1033	42.64	–
XVII	C_2H_5	CN	" " cyanide	Oil	66	0.3042	0.1921	54.45	54.27
						0.3101	0.1953	54.35	–
XVIII	C_2H_5	CNS	" " thiocyanate	80.5-81	82	0.3207	0.1848	49.70	49.94
						0.3210	0.1849	49.67	–
XIX	H		Di-(3-hydroxyalkyl)mercury	113-114	90	0.2831	0.1533	46.70	46.58
						0.2799	0.1510	46.52	–
XX	CH_3		Di-(3-methoxyalkyl)mercury	59-59.5	85	0.2948	0.1492	43.64	43.74
						0.2869	0.1457	43.80	–
XXI	C_2H_5		Di-(3-ethoxyalkyl)mercury **	52-52.5	82	0.2801	0.1341	41.28	41.22
						0.2748	0.1321	41.44	–

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* Found %: N 4.48, 4.38. Calculated %: N 4.10.

** Found %: C 44.63, 44.65; H 7.88, 8.02. Calculated %: C 44.38; H 7.80.

were recrystallized from petroleum ether or alcohol.

Symmetrization of 3-Hydroxy-,3-Methoxy-, and 3-Ethoxy-2,2,3-trimethylbutyl Mercuric Acetates [3].

A solution prepared from 25 ml of a 40% sodium hydroxide solution and 10 g of $SnCl_2 \cdot 2H_2O$ in 5 ml of water was added with continuous efficient stirring to a solution of the hydroxyalkyl mercuric acetate (I; 6 g) or to an emulsion of the methoxy alkyl mercuric acetate (VII; 6.1 g) and the ethoxyalkyl mercuric acetate (XIII; 6.4 g) in water (60 ml). The mixture was stirred for one hour more; the dark precipitate was filtered, washed with water, and extracted with acetone. Water was added to the acetone solution until cloudiness appeared. The crystals which separated on cooling, were dried over calcium chloride and recrystallized from ethyl alcohol.

Di-(3-hydroxyalkyl)mercury (XIX), and the corresponding methoxy (XX), and ethoxy compounds (XXI) (alkyl = 2,2,3-trimethylbutyl) were readily soluble in acetone.

Comparison of the melting points of the γ-mercury alcohols and their methyl and ethyl ethers makes possible the following conclusions.

1. Each of the organo-mercury compounds obtained containing a methoxy group [3-methoxyalkyl mercuric salts and di-(3-methoxyalkyl)mercury] have a higher melting point than the corresponding compounds.

2. Of the organo-mercury compounds containing a hydroxy group, 3-hydroxyalkyl mercuric acetate, chloride, and cyanide, as well as di-(3-hydroxyalkyl) mercury, melt higher than the corresponding methoxy compounds, whereas the melting points of 3-hydroxy- and 3-methoxyalkyl mercuric bromides, iodides, and thiocyanates are characterized by the reverse relationship.

3. The fact must be especially mentioned that, whereas in the 3-methoxyalkyl mercuric series and the 3-ethoxyalkyl mercuric series the melting point of the salts increases in going from the acetate to the chloride, to the bromide, and then to the iodide, the iodide in the 3-hydroxyalkyl mercuric series does not follow this rule; the melting point of the iodide is lower than the temperature of the bromide of this organo-mercury compound.

SUMMARY

1. Cleavage of the three-membered ring occurs by the action of mercuric acetate in water or in alcohol (methyl and ethyl) on the cyclopropane hydrocarbon (1,1,2,2-tetramethylcyclopropane), 3-hydroxyalkyl mercuric acetate, and 3-methoxy- and 3-methoxyalkyl mercuric acetates, respectively are formed (alkyl = 2,2,3-trimethylbutyl).

2. 3-Hydroxy-, 3-methoxy-, and 3-ethoxy-2,2,3-trimethylbutyl mercuric chlorides, bromides, iodides, cyanides, and thiocyanates were obtained by the substitution reaction of the acetates with KCl, KBr, KI, KCN, and KCNS.

3. Symmetrization products, di-(3-hydroxyalkyl)mercury, di-(3-methoxyalkyl)mercury, and di-(3-ethoxyalkyl)mercury(alkyl = 2,2,3-trimethylbutyl) were obtained by the action of an alkaline solution of sodium stannite on 3-hydroxy-, 3-methoxy-, and 3-ethoxy-2,2,3-trimethylbutyl mercuric acetates.

4. Certain generalizations were established for the organo-mercury compounds synthesized on the change of the melting point in relation to the nature of the anion combined with the mercury, and the nature of the functional groups (OH, OCH_3, OC_2H_5) bound to the γ-carbon atoms.

5. All of the sythesized organo mercury compounds (21 preparations), except (I) and (II) which were reported in the first communications, are first being reported.

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FORMATION OF ORGANO-METALLIC COMPOUNDS BY THE REACTION OF AROMATIC SILANES WITH METALLIC CHLORIDES

II. FORMATION OF ORGANO-IRON COMPOUNDS BY THE REACTION OF PHENYLCHLOROSILANES WITH FERRIC CHLORIDE

A. Ya. Yakubovich and G. V. Motsarev

There is no data in the literature on the cleavage of aromatic silanes with ferric chloride. The single case of a related transformation was reported by Manulkin who showed that $FeCl_3$ was able to cleave tetraethylsilane with the formation of triethylchlorosilane [1].

The reaction of $FeCl_3$ with aromatic silanes was investigated with phenyltrichlorosilane and diphenyldichlorosilane as examples. Phenyltrichlorosilane, in contrast to its behavior with $AlCl_3$, does not react with anhydrous $FeCl_3$ even at 250°. On the other hand, the reaction of diphenyldichlorosilane with anhydrous $FeCl_3$ occurs extremely readily and proceeds at temperatures below 0°. The presence in the products of the reaction (at 30-35°), independent of the molar ratio of the reagents, of phenyltrichlorosilane and the absence of $SiCl_4$ indicate that $FeCl_3$ can act upon the diphenyldichlorosilane with the rupture of only one Si—C linkage. Other products of this reaction are either benzene at molar ratio of the reagent or chlorobenzene with an excess of $FeCl_3$.

Therefore, the reaction of phenylchlorosilanes with $FeCl_3$ partly resembles their reaction with $AlCl_3$, but the dearylating action of $FeCl_3$ is expressed more weakly in comparison to $AlCl_3$. Another peculiarity of the action of $FeCl_3$ on phenylchlorosilanes is the fact that, during cleavage of diphenyldichlorosilane with an excess of $FeCl_3$, the phenyl radical which is cleaved is transformed into chlorobenzene, while with molar ratios of the reagents, the phenyl radical which is cleaved is transformed into benzene.

Naturally, the question arises: is the mechanism of cleavage of diphenyldichlorosilane with $FeCl_3$ analogous to the mechanism of the cleavage with $AlCl_3$? In the last case, as it was shown previously [2], the cleavage is accompanied by the formation of the corresponding alumino-organic compounds. There are no doubts on the possibility of the formation of organo-aluminum compounds since these compounds can form and exist at ordinary conditions [3], whereas until recently [4], all attempts to synthesize the analogous organo-iron compounds had ended in failure. However, the absence of metallo-organic compounds of elements of the VIII group of the periodic system which are stable under ordinary conditions, with the exception of cobalt [5], does not exclude the possibility of the formation of these compounds in reactions as intermediate products [6].

If the existence of unstable organo-iron compounds is assumed, a simpler and more natural explanation of the reaction occurring between ferric chloride and phenylchlorosilanes is possible. Actually, if the reaction between $FeCl_3$ and diphenyldichlorosilane proceeds according to the scheme:

$$(C_6H_5)_2SiCl_2 + FeCl_3 \longrightarrow C_6H_5SiCl_3 + [C_6H_5FeCl_2],$$

then the phenyl iron dichloride formed must split, forming ferrous chloride and a phenyl radical, which must be transformed either into diphenyl, or by the addition of hydrogen, into benzene. The formation of diphenyl was not observed in these experiments, but benzene was formed in yields up to 35% of the theoretical. The source of hydrogen in this case, apparently, must be either the phenylchlorosilane*, or moisture introduced in the reaction mixture along with the $FeCl_3$. Thus if the cleavage of diphenyldichlorosilane is effected in the presence of anhydrous $FeCl_3$ and $FeCl_3 \cdot 2.5\,H_2O$ taken in a ratio corresponding to the formation of ferric chloride monohydrate, then the yield of benzene is somewhat increased (to 37.5%).

Naturally, with an excess of $FeCl_3$, the formation of chlorobenzene under the conditions of this reaction should have been expected by means of the reaction:

$$[C_6H_5FeCl_2] + FeCl_3 \longrightarrow C_6H_5Cl + 2FeCl_2$$

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* See, for example, the formation of mercaptans by the thermal cleavage of diphenyldisulfide [7].

or

$$[C_6H_5^{\cdot}] + FeCl_3 \longrightarrow C_6H_5Cl + FeCl_2$$

It was shown experimentally that, by the action of 2.25 moles of $FeCl_3$ on 1 mole of diphenyldichlorosilane, exactly 2 moles of $FeCl_3$ are converted into $FeCl_2$; chlorobenzene is obtained in a yield of 20%. The low yield of the chlorobenzene is explained, evidently, by the condensing action of $FeCl_3$ leading to the formation of solid tars found in the reaction mixture.

It is known that certain organic compounds of metals (for example silver, copper) exist only at temperatures considerably below 0°; such compounds decompose upon raising the temperature All of the reported attempts to synthesize organo-iron compounds were limited to experiments at usual temperatures, which possibly, also explains the negative results of these experiments from the point of view of answering the question of the possibility of existance of organo-iron compounds.

Studying the above question, attempts were made with several experiments to realize the synthesis of organo-iron compounds. For this purpose, the reaction of C_6H_5MgBr with anhydrous $FeCl_3$ was studied at -80° in absolute ether. The results of these experiments led to the conclusion that all of the ferric chloride was transformed at low temperature into $C_6H_5FeCl_2$ by the action of C_6H_5MgBr, which decomposed upon heating to form diphenyl(yield 70.0%) of the theoretical).

$$C_6H_5MgBr + FeCl_3 \longrightarrow [C_6H_5FeCl_2] + MgBrCl$$

$$2[C_6H_5FeCl_2] \longrightarrow (C_6H_5)_2 + 2FeCl_2.$$

By the action of C_6H_5MgBr upon $FeCl_3$ under the usual conditions with an excess of the latter (for 1 mole of C_6H_5MgBr, 2 moles $FeCl_3$), the reaction product is chlorobenzene (yield, 40.0%) in addition to tars:

$$C_6H_5MgBr + FeCl_3 \longrightarrow [C_6H_5FeCl_2] + MgBrCl$$

$$[C_6H_5FeCl_2] + FeCl_3 \longrightarrow C_6H_5Cl + 2FeCl_2.$$

These observations give a basis for the existance of phenyl-dichloroiron in solutions at temperatures about -80°. In order to completely prove the above, an experiment was conducted on the cleavage of diphenyldichlorosilane with anhydrous $FeCl_3$ at -80°; acetyl chloride was added to the reaction mixture at this temperature. Acetophenone, in a yield of 63% of the theoretical based on the diphenyldichlorosilane cleaved, was isolated from the reaction products.

If the ease with which acetophenone is formed by the reaction of $C_6H_5AlCl_2$ with CH_3COCl [2], is considered, then there are no doubts that the reaction in the above case proceeds by an analogous scheme with the participation of $C_6H_5FeCl_2$.

$$(C_6H_5)_2SiCl_2 + FeCl_3 \longrightarrow C_6H_5SiCl_3 + [C_6H_5FeCl_2]$$

$$[C_6H_5FeCl_2] + CH_3COCl \longrightarrow C_6H_5COCH_3 + FeCl_2.$$

EXPERIMENTAL

Reaction of Phenyltrichlorosilane with $FeCl_3$.

7.64 g (0.047 mole) of freshly prepared anhydrous ferric chloride was added to 10.0 g (0,047 mole) of phenyltrichlorosilane. The mixture was heated for 4 hours at 240-250°. The reaction product was extracted with ether, the ether was removed, and the residue was distilled at atmospheric pressure. 9.0 g of colorless liquid with a sharp odor was obtained; b.p. 195-200°.

Found %: Cl 49.7, 49.8; Si 13.0, 13.1. $C_6H_5SiCl_3$. Calculated %: Cl 50.3; Si 13.2.

The solid residue from the distillation was decomposed with water after treatment with ether, and acidified with sulfuric acid. After steam distillation, the aqueous distillate was extracted with ether; no organic products were found in the ether extracts.

Reaction of Diphenyldichlorosilane with $FeCl_3$.

a) Preparation of benzene by the reaction of diphenyldichlorosilane with anhydrous $FeCl_3$. 3.5 g (0.021 mole) of freshly prepared anhydrous ferric chloride was added to 5.4 g (0.021 mole) of diphenyldichlorosilane cooled to -10°. Heating and darkening of the mixture occurred upon the addition of the ferric chloride. the mixture was allowed to stand at 25-30° for 6 hours. The mixture, cooled to -30°, was decomposed with water, acidified with sulfuric acid, (the decomposition proceeded violently with great evolution of heat), and steam distilled. The distillate was extracted with ether, and the ether extracts were dried over calcium chloride. The ether was removed; the benzene (0.6 g) remaining was converted into a crystalline substance by a nitrating mixture, which were yellow crystals with m.p. 89.6° after two recrystallizations from alcohol, which was m-dinitobenzene. Yield 79.8% of the theoretical. The yield of benzene, therefore, was 35% based on the diphenyldichlorosilane reacted.

The residue in the flask after steam distillation (1.8 g) was a transparent yellow tar which corresponded to a tar formed from phenyltrichlorosilane according to analysis for silicon (Found silicon 21.1%, calculated 21.7%). Yield of phenyltrichlorosilane, judging by the amount of tar obtained, was 68% based on the diphenyldichlorosilane used for the reaction.

b) Preparation of benzene by the reaction of diphenyldichlorosilane with $FeCl_3$ monohydrate. 6.55 g (0.032 mole) of $FeCl_3 \cdot 2 \cdot 5H_2O$ and 5.13 g (0.032 mole) of freshly prepared anhydrous ferric chloride was added to 8.0 g of diphenyldichlorosilane. The mixture was heated for 7 hours at 60-70°. The reaction product was vacuum distilled at room temperature. 0.9 g of benzene (b.p. 80-81°, d_4^{20} 0.877; yield 37.5% of the theoretical) was obtained in the receiver cooled with acetone-carbon dioxide mixture (-80°). The benzene was converted into m-dinitrobenzene with m.p. 90.3°. No benzene could be detected in the products of the reaction of diphenyldichlorosilane (8.0 g) with only the hydrate $FeCl_3 \cdot 2.5H_2O$ (7.55 g, i.e., 15% excess), all other conditions being equal.

c) Preparation of acetophenone. 3.2 g (0.019 mole) of freshly prepared anhydrous ferric chloride was added to 5.0 g (0.02 mole) of diphenyldichlorosilane cooled to -80°. The reaction mixture darkened gradually and assumed an intense orange-yellow color, but still remained transparent. The mixture was left to stand in a flask equipped with a calcium chloride tube for 50 hours at -80°, and then 3.0 g (0.038 mole) of acetyl chloride, cooled to -60°, was added to it. The mixture was kept at -70° for 4 hours; then it was poured into cold water The reaction products were extracted with ether, the ether solution was washed with water, and dried over calcium chloride. The ether was removed. The product remaining after the removal of the ether was an oil which crystallized upon standing (0.6 g). The melting point of the crystals separated from the frozen oil at -5°, was 20.7° after recrystallization from petroleum ether. The acetophenone obtained was identified by means of the semicarbazone; m.p. 200°. The yield of acetophenone was 25% of the theoretical based on the amount taken for the reaction, and 63% based on the diphenyldichloride cleaved. The yield of the semicarbazone was 69% of the theoretical.

The residue in the distillation flask (2.0 g) was a transparent, light-yellow tar which corresponded to that obtained from a mixture of diphenyldichlorosilane (60%) and phenyltrichlorosilane (40%) according to analysis for silicon.

0.2096, 0.2148 g substance: 0.0766, 0.0789 g SiO_2 Found %: Si 17.1, 17.2. $(C_6H_5SiO_{1.5})_n$ Calculated %: Si 21.7. $[(C_6H_5)_2SiO]_n$. Calculated %: Si 14.1.

d) Preparation of chlorobenzene and phenyltrichlorosilane. 6.3 g (0.024 mole) of diphenyldichlorosilane was added to a mixture of 10.0 g (0.061 mole) of freshly prepared anhydrous ferric chloride and 21.5 g of cyclohexane (as a solvent) cooled to 0°. The mixture was heated for 7 hours at 35-40° on the water bath. The liquid part was separated by filtration after cooling from the solid residue which was washed with cyclohexane. The filtrate combined with the wash liquor, was distilled through a dephlegmator. The following fractions were obtained: I- b.p. 78-90°, 20.0 g; II- b.p. 90-120°, 1.0 g; III- b.p. 120-145°, 0.9 g; IV- b.p. 145-210°, 3.4 g; 4.5 g of a brown tar remained as a residue.

Fraction I was cyclohexane. Upon the redistillation of Fraction III, 0.5 g of chlorobenzene with b.p. 130-133°, d_4^{20} 1.1047, and chlorine content of 30.7% (calculated chlorine, 31.5%). Yield 20% of the theoretical. The chlorobenzene obtained was transformed into p-chloronitrobenzene with m.p. 82.1°.

Upon redistillation of Fraction IV, 2.7 g of a liquid with a sharp odor (b.p. 198-201°) was obtained which was phenyltrichlorosilane. Yield 52% of the theoretical.

Found %: Cl 49.8; Si 13.1. $C_6H_5SiCl_3$. Calculated %: Cl 50.3; Si 13.2.

The solid brown residue after separation from the liquid, was decomposed by the addition of sulfuric acid (with water cooling). No organic substances were found after steam distillation, and extraction of the distillate with ether.

Reaction of Phenyl Magnesium Bromide with $FeCl_3$.

a) Preparation of chlorobenzene. A solution of phenyl magnesium bromide in 50 ml of ether (phenyl magnesium bromide was prepared from 6.5 g of bromobenzene and 1.1 g of magnesium) was added slowly with efficient stirring and cooling to a mixture of 13.3 g (0.082 mole) of freshly prepared anhydrous $FeCl_3$ and ether. As the reaction proceeded with strong heating, the contents of the flask were periodically cooled to 35-40°. After the addition of all of the phenyl magnesium bromide, the mixture was heated for a half hour at 50-60°, and then was decomposed with water with cooling (-10°). The ether layer was separated, dried, the ether removed, and the residue distilled on an oil bath. After several redistillations, a fraction was obtained with b.p. 130-132° and d_4^{20} 1.107, which corresponded to chlorobenzene by analysis for chlorine (31.3%). Yield 1.4 g, or 40% of the theoretical. The residue in the distillation flask (2.5 g) was a viscous brown tar which did not contain diphenyl.

b) Preparation of diphenyl. A mixture of a solution of 12.3 g (0.076 mole) of freshly prepared anhydrous ferric chloride in 100 ml of ether and a solution of phenyl magnesium bromide in 100 ml of ether (C_6H_5MgBr was prepared from 11.0 g or 0.07 mole of bromobenzene and 2.0 g of magnesium) was kept for 1 hour at -80°, gradually brought to room temperature, decomposed with water, and the reaction products steam distilled. The aqueous distillate was extracted with ether. Diphenyl with m.p. 69.4° was isolated from the ether layer. Yield 7.5 g or 68% of the theoretical.

SUMMARY

1. The reaction of ferric chloride with phenyltrichlorosilane and diphenyldichlorosilane was studied. It was found that diphenyldichlorosilane, in contrast to phenyltrichlorosilane, reacted very readily with $FeCl_3$, cleaving one phenyl radical.

2. The mechanism of the cleavage reaction of diphenyldichlorosilane with ferric chloride was examined, in which the existence of unstable organo-iron compounds as intermediate products was assumed.

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*See Consultants Bureau Translation, p. 805.

Structure of Cobaltic and Nickel Hydroxide Precipitates – p. 941.

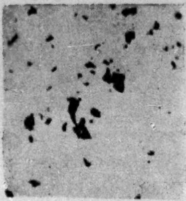


Fig 1. $Co(OH)_3$ precipitated from $CoCl_2$ solution with sodium hypochlorite at 80°. X 90.

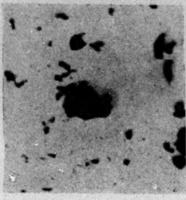


Fig. 2. $Co(OH)_3$ precipitated from $CoSO_4$ solution by sodium hypochlorite at 20°. X 90.

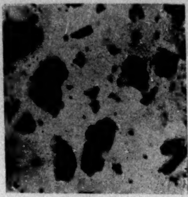
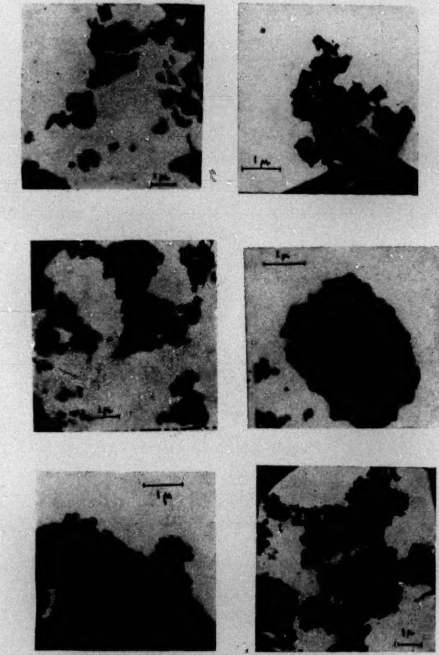


Fig. 3. $Co(OH)_3$ precipitated from a $CoSO_4$ solution at 80° with sodium hypochlorite. X 90.



Figs. 4, 5, 6, 7, 8, 9. Electronograms of the $Co(OH)_3$ residue precipitated from a chloride solution with sodium hypochlorite at 80° Magnification 6.5-9 thousand.

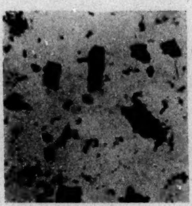


Fig. 10. Higher nickel hydroxide residue obtained by precipitation from a sulfate solution at 20°. X 80

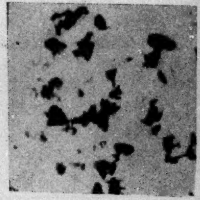


Fig. 11. Higher nickel hydroxide residue obtained by precipitation with sodium hypochlorite from a sulfate solution at 80°. X 80.

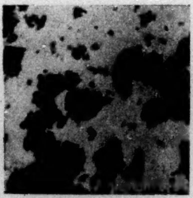
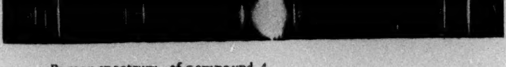


Fig. 12. Friable aggregates formed in initial stage of the process of coagulation of primary precipitates of the higher nickel hydroxides, precipitated from a sulfate solution at 80° X 80.

Fig. 13. Condensation of aggregates obtained as a result of the coagulation of the primary residue of higher nickel hydroxide precipitated from a sulfate solution at 80°.

Action of a Saturated Solution of Cuprous Chloride in Hydrochloric Acid on Dimethylvinylcarbinol – 1041



Raman spectrum of compound 4.

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